AD_____

Award Number DAMD17-95-2-5012

TITLE: Postdoctoral Research Associateship Program with USAMRMC

PRINCIPAL INVESTIGATOR: Judith K. Nyquist, Ph.D.

CONTRACTING ORGANIZATION: National Academy of Sciences
Washington, DC 20418

REPORT DATE: October 1999

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PREPARED FOR: U.S. Army Medical Research and Materiel Command
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FOREWORD

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N/A In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

N/A For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

N/A In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

N/A In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

N/A In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

Judith Nyquist, Ph.D.

PI - Signature Date

Table of Contents

NATIONAL RESEARCH COUNCIL

Resident Research Associateship Program

with the

U.S. Army Medical Research and Materiel Command

Annual Status Report

PUBLICITY

The National Research Council (NRC) Resident Research Associateship Programs for the reporting period were announced to the scientific community in the fall of the preceding year, 1997. Publicity materials describing the NRC-AMRMC Program were distributed in November to presidents, graduate deans, heads of appropriate science and engineering departments of all academic degree-granting institutions in the United States. These materials were also sent to Laboratory Program Representatives, Associateship Advisers, and other interested persons. The publicity materials and other related information were made available on the Internet as well. In addition, Program Staff attended numerous annual society meetings to promote the various programs and meet with prospective applicants through out the year.

REQUESTS

Application materials were distributed in response to specific requests for information about the NRC-AMRMC Associateship Program or as a result of general requests by persons whose fields of specialization appeared to be appropriate for the research opportunities available in the AMRMC laboratories.

COMPETITION

Panel reviews of applicants for the Associateship Programs, including those with the U.S. Army Medical Research and Materiel Command, are conducted in February, June, and October of each year. The following is a breakdown of the action taken with the applications during the period of the report.

	Oct 98	Feb 99	Jun 99	Total
Total Applications	9	16	9	34
Actions taken on the applications:				
Application Ineligible	-	1	-	1
Incomplete/Missing Documentation	1	1	1	3
Application Not Approved/Reviewed by Lab	-	-	1	1
Active Application Pending Lab Response	-	2	-	2
Number of Applications Reviewed	8	12	7	27
Actions taken on the reviewed applications:				
Non-Recommended	1	4	2	7
Recommended	7	8	5	20
Actions taken on Recommended Applications:				
Applicant Accepted Award	5	6	4	15
Applicant Declined the Award	1	1	1	3
Applicant Withdrew After Review/Recommended	1	-	-	1
Alternate with Final Turndown	-	1	-	1

ASSOCIATES' ACTIVITIES

Associates who ended tenure during the report period were on tenure for an average of 30 months, ranging from 12 months to 42 months.

Of the 20 Associates who completed their tenure during the report period, 13 (65%) submitted reports. In their termination reports, the Associates indicated the following scholarly activity while on tenure as an Associate.

49	Domestic Presentations	32	Published Articles in Refereed Journals
16	International Presentations	-	Patents applied for

After completing their tenure Associates, indicated their future plans as follows:

1	Research - National government	-	Non-Profit
1	Administration- government lab	1	Self-employed
7	Remain at Host Agency	1	Unemployed
-	Different NRC Sponsoring Agency	-	Industry
-	Academic -- College or University	-	Post-Doctoral Appointment
-	Student	9	Other/No Information Provided

In their final reports, the Associates were asked to evaluate certain aspects of their experiences on a scale of 1 (low) to 10 (high). The average rating for each item follows:

9.0	Career: Of what value was the NRC experience to your career?
8.7	Lab: What is your evaluation of your experience in the laboratory?
9.5	NRC: What is your evaluation of your interaction with the NRC?

Advisers were also asked to complete an evaluation of the Associate. The following summarizes the Adviser evaluations for Associates completing tenure during the report period. Of the 20 number of Associates, 4 (20%) Adviser evaluations were completed. Assessments were made on four criteria using the following rating scale, 1-Below Average, 2-Average, 3-Above Average, 4-Good, and 5-Outstanding, Exceptional. The average rating for each item follows:

4.8	*Knowledge in Field*	4.8	*Research Techniques*
4.8	*Independence*	5.0	*Motivation.*

The Adviser was asked, "Would you like this Associate as a Professional Colleague?" The following is a breakdown of the Adviser's response.

4	100%	*Yes*
-	0%	*No*

Other information about the Associates' activities can be found in the attachments and appendix.

ASSOCIATES' Citizenship

Associates on tenure as of October 1, 1999 are citizens of the following countries:

Albania	1	Kenya	1
People's Republic of China	1	Mexico	1
Ghana	1	Peru	1
Hungary	1	Portugal	1
India	2	Russia	1
Israel	3	United States	4

Description of Attachments

Attachment 1 is a list of Associates who completed their appointments during the period of October 1, 1999 through September 30, 1999. It includes the Associates' laboratory location, their starting and termination dates, and the names of their Advisers. Associates are required to submit reports upon termination (attached to this report), and Advisers are asked to submit a final evaluation of each Associate. Associates who have not submitted a termination report have received a follow-up letter.

Attachment 2 provides a roster of Associates on Tenure as of October 1, 1999. This listing includes the Associate's Adviser, laboratory location, start and expected termination date, and country of citizenship.

Attachment 3 lists the applicants who received awards during the period of October 1, 1999 through September 30, 1999. It includes the title of their Research Proposals.

Attachment 4 provides a roster of all recommended candidates by category (i.e. accepted, no funding, etc.). This report includes information about the recommended Ph.D. school, proposed research, starting date and Adviser.

Attachment 5 details a cross tabulation of how many Associates were on tenure for the year by center for each quarter within the report period and other yearly periods.

If any of the Associates ending tenure applied for patents, this information is listed in *Attachment 6.*

The *Appendix* contains the copies of the "Final Reports" received from Associates completing their awards during this period.

Associates Who Ended Tenure 10/1/1998 - 9/30/1999

Attachment 1

AMRMC - Medical Res Inst of Chemical Defense

Associate Name+ / Adviser	Division	Tenure Dates Start	Tenure Dates End	Termination Report	Adviser Report
Keller, James Erich Dr. Michael Adler	Pharmacology Division	7/01/96	8/31/99	Not Recd	Not Recd

1 Associates Listed

*** End of Center ***

+ (S) indicates the associate was a Senior.

Associates Who Ended Tenure 10/1/1998 - 9/30/1999

Attachment 1

AMRMC - Medical Research Institute for Infectious Diseases

Associate Name+ Adviser	Division	Tenure Dates Start	Tenure Dates End	Termination Report	Adviser Report
Chen, Shin-Lin Dr. John W Huggins	Virology Division	10/01/97	10/16/98	Received	Received
Guttieri, Mary Charity Dr. Connie S Schmaljohn	Virology Division	10/06/95	11/05/98	Received	Received
Hatfill, Steven Jay(S) Dr. John W Huggins	Virology Division	9/18/97	9/17/99	Received	Received
Kamrud, Kurt Iver Dr. Connie S Schmaljohn	Virology Division	8/05/96	6/30/99	Received	Not Recd
Xiang, Charlie Chunsheng(S) Dr. Kevin Anderson	Virology Division	5/15/98	6/30/99	Not Recd	Received

5 Associates Listed

*** End of Center ***

+ (S) indicates the associate was a Senior.

Associate Name+ Adviser	Division	Tenure Dates Start	End	Termination Report	Adviser Report
Moran, Daniel Sender Dr. Kent B Pandolf	Divison not specified	8/01/97	7/31/99	Received	Received

1 Associates Listed

*** End of Center ***

+ (S) indicates the associate was a Senior.

Associates Who Ended Tenure 10/1/1998 - 9/30/1999

Attachment 1

AMRMC - Walter Reed Army Institute of Research

Associate Name+ Adviser	Division	Tenure Dates Start	Tenure Dates End	Termination Report	Adviser Report
Chakrabarti, Arun Kumar(S) Dr. Prabhati Ray	Division Of Experimental Therapeutics	5/30/96	12/14/98	Received	Received
Cui, Ping Dr. Frank C Tortella	Division Of Neuropsychiatry	7/28/97	7/01/99	Received	Not Recd
Feaster, Shawn Ray Dr. Bhupendra P Doctor	Division Of Biochemistry	2/03/97	2/02/99	Not Recd	Not Recd
Fegeding, Konstantin V. Dr. Jeenan Tseng	Division Of Pathology	10/16/95	1/15/99	Received	Not Recd
Guebre Xabier, Mimi(S) Dr. Urszula Krzych	Division Of Commun Diseases/Immunology	5/20/96	8/31/99	Not Recd	Not Recd
Li, Guo Dr. Harry Zwick	Med Res Detachment-Laser Res, TX	9/16/96	9/15/99	Received	Not Recd
Lumley, Lucille Ann Dr. James L Meyerhoff	Division Of Neuropsychiatry	1/03/96	1/02/99	Received	Received
Luo, Chunyuan Dr. Bhupendra P Doctor	Division Of Biochemistry	3/12/96	3/11/99	Received	Received
Ma, Da Dr. Mustapha Debboun	Division Of Commun Diseases/Immunology	1/29/97	12/28/98	Received	Received
Palmer, Dupeh Rachel O Dr. Urszula Krzych	Division Of Commun Diseases/Immunology	11/27/95	5/26/99	Not Recd	Not Recd
Peel, Sheila Anne Dr. Rodger K Martin	Division Of Experimental Therapeutics	8/01/96	7/31/99	Received	Received
Phillips, James Boyce, Jr Dr. Frank C Tortella	Division of Neurosciences	10/06/97	7/16/99	Received	Not Recd
Yadava, Anjali Dr. Christian F Ockenhouse	Division Of Commun Diseases/Immunology	1/02/96	1/01/99	Received	Not Recd

13 Associates Listed

*** End of Center ***

+ (S) indicates the associate was a Senior.

Associate Name+ Adviser	Division Citizenship	Starting Date	Ending Date
Cerasoli, Douglas Mark Dr. David E Lenz	Pharmacology Division United States	7/20/98	7/19/00
*Kan, Robert Kwai Dr. John P Petrali	972500 Not found United States	5/10/99	5/09/00
Price, Elvis Odin Dr. Ming L Shih	Pharmacology Division United States	1/15/98	1/14/01

*Indicates that the associate started tenure between 10/1/1998 and 9/30/1999.
(S) Associate is a Senior.

Associate Name+ Adviser	Division Citizenship	Starting Date	Ending Date
Ahmed, Syed Ashraf (S) Dr. Leonard A Smith	Toxinology Division United States	8/18/97	8/17/00
*Bosio, Christopher Francis Dr. Jonathan F Smith	Virology Division United States	2/04/99	2/03/00
Dailey, Frank (S) Dr. Arthur M Friedlander	Bacteriology Division United States	11/13/96	11/12/99
*Dekonenko, Alexander Evgenievich Dr. Connie S Schmaljohn	Virology Division Russia	11/02/98	11/01/00
Erwin, James Lawrence Dr. Tran C Chanh	Pathology Division United States	8/10/98	8/09/00
Hensley, Lisa Ellen Dr. Peter B Jahrling	Pathology Division United States	9/01/98	8/31/00
Jensen, Melody Janet (S) Dr. Leonard A Smith	Toxinology Division United States	8/10/98	8/09/00
Khan, Akbar S. (S) Dr. Robert G Ulrich	Toxinology Division United States	9/15/98	12/17/99
Ruff, Albert Leonard Dr. Connie S Schmaljohn	Virology Division United States	3/30/98	10/22/99
Weeks, Steven Douglas Dr. Susan L Welkos	Bacteriology Division United States	5/04/98	5/03/00
Wilson, Julie Ann Dr. Mary K Hart	Virology Division United States	3/24/97	3/23/00

*Indicates that the associate started tenure between 10/1/1998 and 9/30/1999.
(S) Associate is a Senior.

Associate Name+ Adviser	Division Citizenship	Starting Date	Ending Date
*Liu, Liang Ming Dr. Michael A Dubick	974000 Not found People'S Republic Of China	4/08/99	4/07/00
*Peng, Daizhi (S) Dr. Michael A Dubick	974000 Not found People'S Republic Of China	1/05/99	1/04/01

*Indicates that the associate started tenure between 10/1/1998 and 9/30/1999.
(S) Associate is a Senior.

Associate Name+ Adviser	Division Citizenship	Starting Date	Ending Date
Jenner, Jennifer Louise Dr. Harris R Lieberman	973000 Not found United States	6/01/98	5/31/00
*Kanjilal, Partha Partim (S) Dr. Richard R Gonzalez	973000 Not found India	8/02/99	8/01/00
*Weyand, Peter Gregory (S) Dr. Reed W Hoyt	973000 Not found United States	9/20/99	9/19/00

*Indicates that the associate started tenure between 10/1/1998 and 9/30/1999.
(S) Associate is a Senior.

Associate Name+ Adviser	Division Citizenship	Starting Date	Ending Date
*Ashani, Yacov (S) Dr. Bhupendra P Doctor	Division Of Biochemistry Israel	8/02/99	8/01/00
Baranyi, Lajos (S) Dr. C. R Alving	Division Of Biochemistry Hungary	6/22/98	6/21/00
*Biba, Edmond Dr. Ai J Lin	Division Of Experimental Therapeutics Albania	6/28/99	6/27/00
Byrd, Wyatt (S) Dr. Frederick J Cassels	Division Of Medicine United States	1/20/98	1/19/00
*Darko, Christian Asare Dr. Jeffrey A Lyon	Division Of Commun Diseases/Immunology Ghana	11/09/98	11/08/00
Dutta, Sheetij Dr. David E Lanar	Division Of Commun Diseases/Immunology India	7/27/98	7/26/00
Fernandez-Prada, Carmen Maria Dr. David L Hoover	Division Of Commun Diseases/Immunology Peru	3/14/97	3/13/00
*Fonseca, Dina Madeira Dr. Richard C Wilkerson	Division Of Commun Diseases/Immunology Portugal	12/15/98	7/31/00
*Guerrero-Ontiveros, Maria de Lourd Dr. Luther E Lindler	Division Of Commun Diseases/Immunology Mexico	2/16/99	2/15/00
*Korolev, Sergey Vasilyevich Dr. Jeenan Tseng	Division Of Pathology Russia	9/01/99	8/31/00
*Leader, Haim Nissan (S) Dr. Richard K Gordon	Division Of Biochemistry Israel	5/10/99	5/09/00
*Tashma, Zev (S) Dr. Bhupendra P Doctor	Division Of Biochemistry Israel	8/02/99	5/01/00
*Troyer, Jill Michelle Dr. Daniel A Strickman	Walter Reed Army Institute of Research United States	1/04/99	1/03/01
Waitumbi, John Njenga (S) Dr. Jose A Stoute	Medical Research Unit-Kenya Kenya	2/09/98	2/08/00
*Zhang, Peng (S) Dr. Peter K Chiang	Division Of Biochemistry People'S Republic Of China	2/01/99	1/31/00

*Indicates that the associate started tenure between 10/1/1998 and 9/30/1999.

(S) Associate is a Senior.

Name/
Research Title

October 1998 Awardees

Awardees Listed 5

Guerrero-Ontiveros, Maria d
Regulation of the Expression of Pathogenic Yersinia Pestis Proteins During Intracellular Association with Macrophages

Kanjilal, Partha P
Dynamic Analysis of Cardiovascular Response and Modelling of Individual Variability by an Optimized Neural Network

Leader, Haim N
Synthesis and Structure of Sime Phosphorylated Oximes Related to Organophosphate Poisoning Therapy

Troyer, Jill M
Identification of Novel Gene Expression and Transcriptional Disparities Among Aedes Aegypti Populations that are Permissive or Refractory to Transmission of the Dengue Virus

Zhang, Peng
Caspase and Cell Death: The Key to Regulate Apoptosis and Control Apoptosis Related Diseases

February 1999 Awardees

Awardees Listed 6

Ashani, Yacov
Chemical Modifications of Human Butyrylcholinesterase

Biba, Edmond
Mechanism Based Design of 1,5-Naphthyridine Analogs of Primaquine and Chloroquine as Potential Antimalarial Compounds

Kan, Robert K
Immunohistochemical and Ultrastructural Identification of Integrins, Basement Membrane Proteins, Cytokines, and Proteases in Human Skin Explants, Following Sulfer Mustard Poisoning

Markotic, Alemka
Role of the Cytokines and Chemokines in the Infection of Human Cells with Hantaviruses

Tashma, Zev
Purification of Human Butyrycholinesterase and Testing of an Appropriate Pharmaceutical Formulation Suitable for Human Use

Weyand, Peter G
Energy Balance and Performance in Extreme Environments

June 1999 Awardees

Awardees Listed 4

Korolev, Sergey V
Development of Staphylococcal Enterotoxin B (SEB) Vaccines Delivered by Lactobacillus Casei

Leon Villalba, Luis R
Identification and Characterization of New Arbovirus Isolates with the Potential of Infecting Human from the South American Amazon Basin

Name/
Research Title

Marvaud, Jean-Cristophe
Development of a Therapeutic Delivery System for Botulism

Zhu, Shuren
Design and Synthesis of Cysteine Proteinases Inhibitor as Potential Activesicant and Antimalarial Agent

Total Associates Listed for Lab 15

October 1998

A- Accepted Award (5 Applicants listed)

GUERRERO-ONTIVEROS, MARIA D — Ph.D. Date: 1998
Citizenship: Mexico — Swiss Federal Inst Tech-Laussanne
Adviser: Dr. Luther E Lindler — Actual Starting Date: 2/16/99
Research Field: Infectious Diseases — Termination Date: 2/15/00
Research Title: Regulation of the Expression of Pathogenic Yersinia Pestis Proteins During Intracellular Association with Macrophages

KANJILAL, PARTHA P — Ph.D. Date: 1983
Citizenship: India — University of Sheffield/England
Adviser: Dr. Richard R Gonzalez — Actual Starting Date: 8/02/99
Research Field: Biomedical Engineering — Termination Date: 8/01/00
Research Title: Dynamic Analysis of Cardiovascular Response and Modelling of Individual Variability by an Optimized Neural Network

LEADER, HAIM N — Ph.D. Date: 1970
Citizenship: Israel — Hebrew Univ of Jerusalem/Israel
Adviser: Dr. Richard K Gordon — Actual Starting Date: 5/10/99
Research Field: Medicinal Chemistry — Termination Date: 5/09/00
Research Title: Synthesis and Structure of Sime Phosphorylated Oximes Related to Organophosphate Poisoning Therapy

TROYER, JILL M — Ph.D. Date: 1996
Citizenship: United States — Old Dominion University/VA
Adviser: Dr. Daniel A Strickman — Actual Starting Date: 1/04/99
Research Field: Entomology — Termination Date: 1/03/01
Research Title: Identification of Novel Gene Expression and Transcriptional Disparities Among Aedes Aegypti Populations that are Permissive or Refractory to Transmission of the Dengue Virus

ZHANG, PENG — Ph.D. Date: 1983
Citizenship: People's Republic of China — Henan Medical University/China
Adviser: Dr. Peter K Chiang — Actual Starting Date: 2/01/99
Research Field: Applied Biology — Termination Date: 1/31/00
Research Title: Caspase and Cell Death: The Key to Regulate Apoptosis and Control Apoptosis Related Diseases

8- Declined

LUGO, DELIA I — Ph.D. Date: 1990
Citizenship: United States — Columbia University/NY
Adviser: Dr. Michael Adler
Research Field: Neurotoxicology
Research Title: Molecular Analysis of Botulinum Toxin Binding and Internalization

W- Withdrew after Review/Recommend

CHANEY, LESLIE A — Ph.D. Date: 1998
Citizenship: United States — University of Mississippi
Adviser: Dr. Tsung-Ming A Shih
Research Field: Pharmacology Toxicology
Research Title: Evaluation of Extracellular Changes in Neurotransmitters in Guinea Pig Brain following the Initiation of Seizures by Soman, and the Therapeutic Potential of Mixed-Acting Cholinergic Antagonists in Preventing Seizures and Neuropathology

February 1999

1- Recommended (2 Applicants listed)

RAZIUDDIN, RAZI — Ph.D. Date: 1981
Citizenship: United States — Banaras Hindu University/India
Adviser: Dr. Arthur M Friedlander
Research Field: Biomedical Science
Research Title: Characterization of Anthrax Gamma Phage and Use in Treatment

SANTIAGO, MELISSA P — Ph.D. Date: 1999
Citizenship: United States — University of Miami/FL
Adviser: Dr. Steven I Baskin
Research Field: Pharmacology Toxicology
Research Title: Pharmacology and Localization of Centrally Acting Organophosphates on Muscarinic Acetylcholine Receptor Subtypes

A- Accepted Award (6 Applicants listed)

ASHANI, YACOV — Ph.D. Date: 1970
Citizenship: Israel — Hebrew Univ of Jerusalem/Israel
Adviser: Dr. Bhupendra P Doctor — Actual Starting Date: 8/02/99
Research Field: Chemical Biology — Termination Date: 8/01/00
Research Title: Chemical Modifications of Human Butyrylcholinesterase

BIBA, EDMOND — Ph.D. Date: 1999
Citizenship: Albania — American University/DC
Adviser: Dr. Ai J Lin — Actual Starting Date: 6/28/99
Research Field: Medicinal Chemistry — Termination Date: 6/27/00
Research Title: Mechanism Based Design of 1,5-Naphthyridine Analogs of Primaquine and Chloroquine as Potential Antimalarial Compounds

KAN, ROBERT K — Ph.D. Date: 1998
Citizenship: United States — The Pennsylvania State University
Adviser: Dr. John P Petrali — Actual Starting Date: 5/10/99
Research Field: Pathology — Termination Date: 5/09/00
Research Title: Immunohistochemical and Ultrastructural Identification of Integrins, Basement Membrane Proteins, Cytokines, and Proteases in Human Skin Explants, Following Sulfer Mustard Poisoning

MARKOTIC, ALEMKA — Ph.D. Date: 1999
Citizenship: Croatia — University of Zagreb/Croatia
Adviser: Dr. Connie S Schmaljohn — Actual Starting Date: 10/25/99
Research Field: Viral Immunology — Termination Date: 10/24/00
Research Title: Role of the Cytokines and Chemokines in the Infection of Human Cells with Hantaviruses

TASHMA, ZEV — Ph.D. Date: 1975
Citizenship: Israel — Hebrew Univ of Jerusalem/Israel
Adviser: Dr. Bhupendra P Doctor — Actual Starting Date: 8/02/99
Research Field: Pharmaceutical Chem — Termination Date: 5/01/00
Research Title: Purification of Human Butyrycholinesterase and Testing of an Appropriate Pharmaceutical Formulation Suitable for Human Use

WEYAND, PETER G — Ph.D. Date: 1992
Citizenship: United States — University of Georgia
Adviser: Dr. Reed W Hoyt — Actual Starting Date: 9/20/99
Research Field: Physiology — Termination Date: 9/19/00
Research Title: Energy Balance and Performance in Extreme Environments

8- Declined

JACOBS, ERIC A — Ph.D. Date: 1997
Citizenship: United States — University of Florida
Adviser: Dr. Gregory Galbicka
Research Field: Neuropsychology
Research Title: Anticholinergic Drug Effects on Complex Discriminations Requiring Rapid Reactions in Rhesus Monkeys

Y- Alternate with Final Turndown

GUPTA, RAJIV — Ph.D. Date: 1999
Citizenship: India — Texas A&M University
Adviser: Dr. M L Pitt
Research Field: Mechanical Engineering
Research Title: Characterization of Bioaerosols and Deposition Studies in Animal Models

June 1999

A- Accepted Award (4 Applicants listed)

KOROLEV, SERGEY V — Ph.D. Date: 1996
Citizenship: Russia — Russia Unknown
Adviser: Dr. Jeenan Tseng — Actual Starting Date: 9/01/99
Research Field: Pathology — Termination Date: 8/31/00
Research Title: Development of Staphylococcal Enterotoxin B (SEB) Vaccines Delivered by Lactobacillus Casei

LEON VILLALBA, LUIS R — Ph.D. Date: 1999
Citizenship: Ecuador — Ohio University
Adviser: Dr. Michael J Turell — Expected Starting Date: 2/01/00
Research Field: Virology and Epidemiology — Termination Date: 1/31/01
Research Title: Identification and Characterization of New Arbovirus Isolates with the Potential of Infecting Human from the South American Amazon Basin

MARVAUD, JEAN-CRISTOPHE — Ph.D. Date: 1998
Citizenship: France — University of Paris-Sud XI/France
Adviser: Dr. Leonard A Smith — Actual Starting Date: 12/01/99
Research Field: Molecular Biology — Termination Date: 11/30/00
Research Title: Development of a Therapeutic Delivery System for Botulism

ZHU, SHUREN — Ph.D. Date: 1997
Citizenship: People's Republic of China — Rice University/TX
Adviser: Dr. Ai J Lin — Actual Starting Date: 11/01/99
Research Field: Medicinal Chemistry — Termination Date: 10/31/00
Research Title: Design and Synthesis of Cysteine Proteinases Inhibitor as Potential Activesicant and Antimalarial Agent

8- Declined

SHI , XIAN — Ph.D. Date: 1996
Citizenship: People's Republic of China — State Univ of New York-Binghamton
Adviser: Dr. Ai J Lin
Research Field: Chemistry
Research Title: Synthesis of Novel Statine-Containing Peptide Fluoromethyl Ketone Protease Inhibitors as Potential Nativesicant and Antimalarial Agents

On Tenure Report by Quarter and Center

For the year starting **October 1, 1998**

Attachment 5

U.S. Army Medical Research and Materiel Command

Center	Number of Associates on tenure as of					
	10/1/97	10/1/98	1/1/99	4/1/99	7/1/99	10/1/99
Medical Res Inst of Chemical Defense	4	3	3	3	4	3
Medical Research Institute for Infectious Diseases	16	14	13	14	12	11
Research Institute of Medical Sciences	-	-	-	-	-	-
U.S. Army Institute of Surgical Research	-	-	-	1	2	2
U.S. Army Research Institute of Environmental Medicine	2	2	2	2	2	3
Walter Reed Army Institute of Research	22	18	18	16	16	15
	44	37	36	36	36	34

[r_tenure_by_quarter]

1) DATE : December 11, 1998

2) NAME : ARUN K CHAKRABARTI

3) NAME OF LABORATORY OR CENTER AND LOCATION : Walter Reed Army Institute of Research, Washington, D.C.

4) DATES OF TENURE : May 30, 1986 -- December 14, 1998

5) TITLE OF RESEARCH PROPOSAL : Biochemical and Molecular Biological Aspects of Vesicating Agents Induced Protease Stimulation

6) NAME OF RESEARCH ADVISER : Dr. Prabhati Ray

7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST?
If so, list position of title and address : No

8) PROFESSIONAL SOCIETY OFFICES HELD DURING TENURE: : None

9) PROFESSIONAL TRAVEL DURING TENURE
List location(s) and date(s) of travel to scientific meetings. List foreign meetings separately : (a) San Francisco, California
December 9-12, 1996.
American Society Of Physiology
(b) New Orleans, LA
FASEB, April 6-9 , 1997
(c) Seattle, Washington
March 1-5 , 1998
American Society of Toxicology
(d) Baltimore, MD
July 3-5, 1998
Bioscience Review Meeting of Army.

10) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES : Walter Reed Army Institute of Research, Washington, D.C., October 22, 1996.

List location(s) and date(s) :

11) SUMMARY OF RESEARCH DURING TENURE
List significant findings in concise form (100 words or less). Please do NOT use Greek letters or mathematical signs and symbols. :

(a) A membrane-bound serine protease induced by Sulfur Mustard (SM) in cultured human epidermal keratinocytes (NHEK) was purified to homogeneity and characterized. Analysis of the purified enzyme revealed a single polypeptide at the 80 kiloDalton region. Physiological protein laminin was found to be good substrate for this enzyme.

(b) A specific, endogenous inhibitor of the above mentioned protease was also purified to homogeneity from NHEK. Analysis of the purified inhibitor revealed a single polypeptide at the 116 Kilo dalton region.

(c) The expression of the novel serine protease induced by SM was also studied by Northern Blot technique. Overall, the results of the present study demonstrate an up-regulation due to *de novo* synthesis of protease in NHEK after treatment with SM which may be modulated by antisense DNA treatment.

12) RESEARCH IN PROGRESS : Cloning and sequencing of the SM-induced protease gene.

13) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH
Provide complete citation(s), including author(s), full name of journal, volume number, page number(s), and year of publication. Please list separately :
(a) Publications in peer-reviewed journals; ---"Purification and Characterization of Sulfur mustard induced

protease from normal human epidermal keratinocytes"

A.K. Chakrabarti, P.Ray, C.A. Broomfield, and R.Ray. Biochemical Pharmacology, 56(4): 467-472, 1998.

(b) Books or book chapters; and
(c) Manuscripts in preparation, manuscripts submitted

: "Purification of a novel endogenous inhibitor of sulfur mustard induced protease from normal human epidermal keratinocytes: possible implication in vesicant intervention"
A.K. Chakrabarti and P.Ray (In Preparation).

"Expression of Sulfur Mustard induced protease in human epidermal keratinocytes-Modulation by antisense DNA" A.K. Chakrabarti, P.Ray and R.Ray (In Preparation).

14) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES
Provide complete reference with author(s), title, abstract or proceeding citation, and meeting name and location for international and domestic

(a) "Isolation, purification and characterization of protease activated in sulfur mustard and nitrogen mustard treated human keratinocytes" -A.Chakrabarti and P. : Ray; The Faseb Journal, Vol. 11, Number 3, Meeting of Experimental Biology, New Orleans, LA, April 6-9, 1997, Page# A366, Abstract# 2123.

(b) "Purification of a novel endogenous inhibitor of sulfur mustard (HD) induced protease in normal human epidermal keratinocytes"- A. Chakrabarti and P.Ray; The Toxicologist , Vol.42, Number 1-S, 37 Th.Annual Meeting at Seattle, Washington, March 1-5, Page # 392, Abstract # 1932.

15) PATENT OR COPYRIGHT

APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH : None

16) FUTURE POSITION TITLE AND STATUS (check as many as apply) : Unemployed

17) FORWARDING ADDRESS : 17708 SILKCOTTON WAY, GAITHERSBURG, MD 20877

18) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS
Comment on the usefulness of the Associateship Programs to you, and include suggestions for improvements : It was beneficial for my research career but I had some bitter experience too. I was forced to do some experiments on screening few chemical compounds to detect their antiprotease activity which was not in the original NRC research proposal. I have to resign 45 days before the tenure because I was extremely mentally tortured by my research adviser who even declined to write a reference letter for me as I am unemployed and looking for a job. I would like to request NRC to take proper steps to prevent this type of situation.

1) Date: 02.08.99

2) Name: Konstantin Valdemarovich Fegeding

3) Name of Laboratory or Center and Location: Dpt. of Experimental Pathology, Div of Pathology

Walter Reed Army Institute of Research, 14th and Dahlia sts., N.W., Washington, DC 20307

4) Dates of Tenure: 10.15.95 - 01.15.99

5) Title of Research Proposal: Cytokines production analysis during course of toxic shock caused by Staphylococcal enterotoxin B (SEB) in mice primed with ActinomicynD (ActD).

6) Name Of Research Adviser: Dr. Jeenan Tseng

7) I am on leave from my professional post. My position is a Senior Staff Researcher, Lab. For Mediators of Immunity and Hematopoiesis, Hematology Research Center, Russian Academy of Medical Sciences, Novozykovsky per. 4a, Moskow, 125167, Russia.

8) Professional Society Offices Held During Tenure: None

9) Professional Travel During Tenure: 04.18-04.23 98 Annual FASEB Meeting, San Francisco, CA.
05.15-05.18.98 Annual Midatlantic Immunology Meeting, Ocean City, MD
06.25-06.27.98 International symposium "Gene Technology in Analysis and Treatment of Malignant and Inherited Human Diseases", Moscow, Russia.

10) Seminars or Lectures Delivered at Universities and/or Institutes: December 1996 Seminar at WRAIR, Washington DC.
April 1997 Seminar at NCI NIH, Frederick, MD.

September 1997 Research Report at USAMRIID, Frederick, MD.
23 March 1998 Research Report at Staphylococcal Entrotoxin Science and Technology Objective External Review Meeting, USAMRIID, Frederick, MD

11) Summary of Research During Tenure: Semiquantitative RT-PCR ELISA approach for measurement of relative amounts of cytokine mRNAs was developed. Total RNA samples were isolated from, liver, lungs and spleen of control (ActD-treated and healthy, SEB-injected) and SEB- intoxicated ActD primed mice sacrificed at 0, 3, 6, 9, 12, 15, 24 hours after SEB-challenge. RNA samples from lungs were subjected to semiquantitative RT-PCR-ELISA for measurement of relative amounts of TNF-a, Il-1b, IFN-g MCP-1, MIP-1a,b, MIP-2, RANTES, TCA-3, LPTN and iNOS mRNAs in the samples. It was shown that intensive transcription of the genes in lung tissue induced by SEB occurred at the earliest stages of toxic shock.

12) Research in Progress. In situ hybridization in frozen lung tissues experiments are in progress now.

Different mutant forms of SEB were created by in vitro mutagenesis for search of possible vaccine. Expression protocols of the mutants in E.coli strains are in stage of development.

Duffy antigen was proposed to be used as therapeutic agent for treatment of SEB-induced toxic shock. Human gene for Duffy-b antigen was cloned and recombinant baculoviruses for expression of the antigen in insects cell lines were constructed. Experiments for optimization of expression of the protein in SF9 insect cell line are in progress.

13) Publications and Papers Resulting from NRC Associateship Research:

C. Feng, W. Zhao, K.V. Fegeding, J. Komisar and Jenan Tseng. "Resistance of **Staphylococcal Enterotoxin B-(SEB-) induced proliferation and apoptosis to the effects of dexamethasone in mouse lymphocyte cultures."**Manuscript in preparation.

14) Presentations at Scientific Meetings or Conferences.

Poster and report at International symposium "Gene Technology in Analysis and Treatment of Malignant and Inherited Human Diseases", Moscow, Russia, 06.25-06.27.98.The title:**Semiquantitative Detection of Cytokine and Chemokine mRNA by RT-PCR in Lungs of Mice During Early Stages of Toxic Shock Induced by Staphylococcal Enterotoxin B (SEB).K.V. Fegeding, J. Chen, J. Komisar and Jeenan Tseng.**

15) Patent or Copyright Applications Resulting from NRC Associateship Research: None

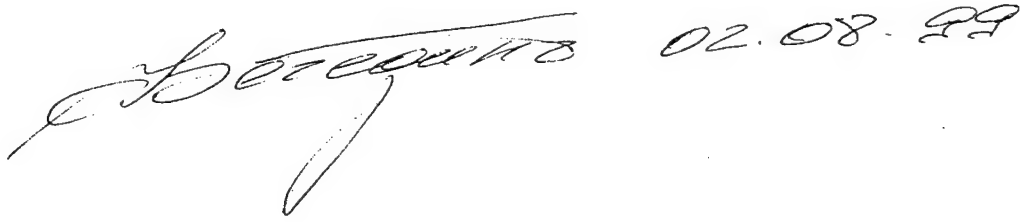
16) Future Position Title and Status:

National Government-Research, Dpt. of Immunology, Walter Reed Army Institute of Research, Self employed.

17) Forwarding Address: 1220 East West Hwy., #1702, Silver Spring, MD, 20910, USA.

18) Appraisal of the Associateship Programs:

I am very grateful for this program. It helps me to bring my research on systemic inflammation on highest modern level. I suggest that 5 years of associateship program could be very helpful for completion of proposed research projects.



NRC RESEARCH ASSOCIATESHIP PROGRAM

DATE: November 2, 1998

NAME: Mary C. Guttieri

LAB OR CENTER: USAMRIID, Ft. Detrick, MD

DATES OF TENURE: October 5, 1995-November 5, 1998

TITLE OF RESEARCH PROPOSAL:

Production and Examination of Mouse and Human Monoclonal Antibodies to Hantaan and Puumala viruses using a Baculovirus Expression System

RESEARCH ADVISOR: Dr. Connie Schmaljohn

LEAVE FROM PROFESSIONAL POST: none

PROFESSIONAL SOCIETY OFFICES: none

PROFESSIONAL TRAVEL:

American Society for Virology 15th Annual Meeting
London, Ontario, Canada
July 13-17, 1996

American Society of Tropical Medicine and Hygiene
Baltimore, Maryland
December 1-5, 1996

SEMINARS OR LECTURES AT UNIVERSITIES AND/OR INSTITUTES: none

SUMMARY OF RESEARCH:

I conducted passive protection experiments in hamsters to determine the protective efficacy of a baculovirus-expressed human monoclonal antibody to Puumala virus. The results of these studies indicated that this antibody does not fully protect animals from challenge with Puumala virus. I conducted an extensive analysis of human hybridomas generated from the spleens of transgenic mice and determined that none secrete Hantaan-specific monoclonal antibodies. I developed a system to select human B cells

producing hantavirus-specific antibodies by using antigen coated magnetic beads. I determined the complete nucleotide sequence of a previously cloned Fc-containing gene region and designed a strategy to construct cassette plasmid vectors containing human signal sequences and an Fc antibody coding region. I conducted extensive analysis of stably-transformed insect cell lines expressing a human IgG MAb to the G2 protein of Puumala virus and developed a strategy to determine the copy number of heavy and light chain antibody genes integrated within transformed insect cell genomes.

RESEARCH IN PROGRESS:

I am completing studies to determine the copy number of heavy and light antibody genes within transformed insect cells. I am analyzing immortalized B cell lines to attempt to identify those expressing hantavirus-specific antibodies. Specific cells of interest will be selected and cloned using magnetic bead technology. I am completing the construction of a combinatorial library using Fab antibody genes amplified from the peripheral blood of a Puumala-virus infected individual. I am beginning construction of Fc cassette plasmid vectors.

PUBLICATIONS AND PAPERS:

(a) Publications in peer-reviewed journals

Liang, M., M. Guttieri, A. Lundkvist, and C. Schmaljohn. 1997. Baculovirus expression of a human G2-specific, neutralizing IgG monoclonal antibody to Puumala virus. *Virology* **235**:252-260.

(b) Books or book chapters

(c) Manuscripts in preparation

Guttieri, M.C., C. Bookwalter, M. Liang, A. Lundkvist, and C. Schmaljohn. 1998. Expression of a human G2-specific, neutralizing monoclonal antibody to Puumala virus in stably transformed lepidopteran cells. (in preparation).

PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES:

Guttieri, M., M. Liang, A. Lundkvist, and C. Schmaljohn. 1996. Baculovirus expression of a human G2-specific, neutralizing monoclonal antibody to Puumala virus. ASV 15th Annual Meeting, London, Ontario, Canada.

Guttieri, M.C., M. Liang, A. Lundkvist, and C.S. Schmaljohn. 1996. Baculovirus expression of a human G2-specific, neutralizing monoclonal antibody to Puumala virus. ASTMH 45th Annual Meeting, Baltimore, MD.

Guttieri, M.C., C.S. Bookwalter, A. Lundkvist, and C.S. Schmaljohn. 1998. Expression of a human G2-specific, neutralizing monoclonal antibody to Puumala virus in stably transformed Lepidopteran cells. Conference on Emergence and Control of Rodent-Borne Viral Diseases, Annecy, France.

PATENT OR COPYRIGHT APPLICATIONS: none

FUTURE POSITION TITLE AND STATUS:

Title: Technical Professional V (government contractor)

Location: USAMRIID, Ft. Detrick--in the laboratory of Dr. Connie Schmaljohn

FORWARDING ADDRESS:

Dr. Mary C. Guttieri
1005-2A Columbine Drive
Frederick, MD 21701

APPRAISAL OF THE ASSOCIATESHIP PROGRAMS:

I am grateful for the research opportunities afforded me by the NRC associateship program. During my tenure, I acquired knowledge and expertise in areas defined as "cutting edge technology", equipping me with valuable research skills in a competitive market. The administrative staff was both very courteous and helpful. Assistance was always offered in a kind and timely manner. As for improvement, I feel that there is a definite need to increase the maximum length of tenure from 3 years to 4 or 5 years. This adjustment would allow for the proper completion of important projects, manuscripts, and presentations.

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

National Research Council
Associateship Programs

REPORT FORM

If you have downloaded this form, enter the information electronically.
Return this form directly to the NRC as an e-mail attachment or print out and mail.

1) NAME

Steven J. Hatfill

2) DATE

August 11, 1999

3) *Program / Agency*	*Lab / Center*	*Location*
or enter abbreviation		
click on prgm/agnc **RIID**	**Antiviral therapeutic**	**USAMRIID**

4) DATES OF TENURE

September 15, 1997 -- to – September 17, 1999

5) NAME OF RESEARCH ADVISER

John Huggins

6) IF YOU ARE ON LEAVE FROM A PROFESSIONAL POST, WILL YOU RETURN TO YOUR PREVIOUS EMPLOYER?

☐ Yes ☒ No

7) PROFESSIONAL AWARDS RECEIVED, SOCIETY OFFICES HELD DURING TENURE

nil

8) PROFESSIONAL TRAVEL DURING TENURE **List locations and dates of travel to scientific meetings; group into domestic and foreign.**

nil

9) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES **List location(s) and date(s).**

Council on Foreign Relations-May 21, 1998
Potomac Institute for Policy Studies/George Washington University-June 16, 1998
Pentagon, Assistant Secretary of Defense SO/LIC-July 14, 1998
Pentagon, Assistant Secretary of Defense for Health Affairs-August 11, 1998
DoD Worldwide Conference on Antiterrorism-August 24,1998

10) TITLE OF RESEARCH PROPOSAL

Pathogenesis of the Coagulopathy associated with Filovirus Infections

11) SUMMARY OF RESEARCH DURING TENURE **Itemize significant findings in concise form (25 words/250 characters each item.) Utilize concepts and key words.**

1) **Identification of early intrinsic pathway coagulation abnormality in Ebola Non-Human Primate infection.**
2) **Documentation of equivelent Ebola-induced coagulopathy in murine and guinea pig models.**
3) **Documentation of pathogenic differences in human tissues infected with Ebola Zaire and Reston strains**
4) **Documentation of transient coagulopathy in Monkeypox infected non-human primates.**
5) **Applications of NASA RWV for advanced Orthopoxvirus research.**
6) **Efficacy of Cidofovir in minimizing pulmonary damage in Orthopoxvirus infection.**
7)
5)

12) RESEARCH IN PROGRESS **Briefly describe in 100 words or less.**

Use of PAGE to document abnormal von Willebrand multimers during early Ebola Zaire induced coagulopathy in non-human primates.
Utilization of the NASA RWV system to study camelpox infection of human lung tissue, and the development of this culture system to document cytokine changes in human lymphoid tissue infected with Orthopoxvirus.

13) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH
Provide complete citation(s) including author(s), full name of journal, volume number, page number(s), year of publication.

(a) Publications in peer-reviewed journals:

(b) Books or book chapters:

Textbook of Aerospace Medicine-USAF-Aeromedical Evacuation

(c) Manuscripts in preparation, manuscripts submitted:

Pathogenic differences between Ebola Reston and Ebola Zaire in the NASA RWV Bioreactor
Coagulation in Mouse, Guinea Pig and Non-Human Primate models of Ebola Zaire
Cidofovir treatment for Orthopoxvirus infections

14) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES
Provide complete reference with author(s), title, abstract/proceeding citation, meeting name, location. Group into domestic and foreign.

Bray,M., Jaax,N., Geisbert,T., Kell,W., Hatfill,S.,Huggins,J. pathogenesis of Lethal Ebola Virus Infection in Adult Immunocompetent Mice. American Society of Virology, Annual Meeting, Vancouver, canada, july 11, 1998.

15) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH
Provide titles, authors, and dates of applications.

nil

16) NEW POSITION STATUS/CATEGORY **Please indicate only one.**

- ☐ *Research -- National Government* (U.S. or Foreign)
- ☐ *Administration -- U.S. Govt.* (Fed., State, or Local)
- ☐ *Continuation at Host Lab/Center*
  Abbreviate Host Lab/Center: _____
- ☐ *College/University*
- ☐ *Postdoctorate*
- ☒ *Self Employment*
- ☐ *Non Profit*
- ☐ *Industry*
- ☐ *Other*
  Please specify:

17) NEW POSITION TITLE AND NAME (not address) OF ORGANIZATION

N/A

18) FORWARDING ADDRESS **(to which your tax statement will be mailed)**

1711 W. 7th Street, Apt 9
Detrick Plaza Apartments
Frederick, MD 21702

19) APPRAISAL OF THE ASSOCIATESHIP PROGRAM
Please evaluate each of the following on a scale of 1 (poor) to 10 (excellent):

10 a) Of what value was this experience to your career?

10 b) What is your evaluation of your experience in the laboratory?

10 c) What is your evaluation of your interaction with the NRC?

Please provide any additional comments on the usefulness of the Associateship Program to you, including suggestions for improvements.

The NRC Associate Program is outstanding and is really a national asset, both with respect to individual career advancement as well as providing assistance to National civilian and Department of Defense research programs.

USPS Mailing Address
Associateship Programs [TJ 2114]
NATIONAL RESEARCH COUNCIL
2101 Constitution Avenue, NW
Washington, DC 20418

FAX Number
202 – 334 – 2759
INTERNET
national-academies.org/rap

Express-Delivery Address
Associateship Programs [Suite 2114]
NATIONAL RESEARCH COUNCIL
1000 Thomas Jefferson Street, NW
Washington, DC 20007

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

REPORT FORM
RESEARCH ASSOCIATESHIP PROGRAMS

If you have downloaded this, you may print out and enter the information manually, or you may enter the information electronically, then return as an e-mail attachment.

1) NAME

Kurt I. Kamrud

2) DATE

June 18, 1999

3) *Program / Agency*	*Lab / Center*	*Location*
or enter abbreviation		
click on prgm/agnc **AMRDC**	**AMRIID**	**Fort Detrick**

4) DATES OF TENURE

August 5, 1996 -- to – **June 30, 1999**

5) NAME OF RESEARCH ADVISER

Dr. Connie Schmaljohn

6) IF YOU ARE ON LEAVE FROM A PROFESSIONAL POST, WILL YOU RETURN TO YOUR PREVIOUS EMPLOYER?

☐ Yes ☒ No

7) PROFESSIONAL AWARDS RECEIVED, SOCIETY OFFICES HELD DURING TENURE

American Committee on Arthropod-borne Viruses, Scherer-Hardy Award - 1997

8) PROFESSIONAL TRAVEL DURING TENURE **List location(s) and date(s) of travel to scientific meetings; group into domestic and foreign.**

American Society for Virology, Monatana, July 1997
American Society of Tropical Medicine and Hygiene, Florida, December 1997
International Conference on Negative Strand Viruses, Ireland, September 1997
International Conference on HFRS and Hantaviruses, Georgia, March 1998
Emergence and Control of Rodent-borne Viral Diseases, France, October 1998
Vaccine Research Conference, Wahington D.C., March 1999

9) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES **List location(s) and date(s).**

University of Deleware , September 1996

10) TITLE OF RESEARCH PROPOSAL

Development and Comparison of Three Recombinant Vaccines to Puumala Virus

11) SUMMARY OF RESEARCH DURING TENURE **Itemize significant findings in concise form. Utilize concepts and key words.**

1) Develop and test DNA-based Sindbis replicon vectors for Hantavirus vaccinces

2) Develop and test DNA-based vectors for Hantavirus vaccines

3) Develop and test packaged Sindbis replicon vector for Hantavirus vaccines

4) Demonstrate protective efficacy of all three vaccine vectors for Hantaviruses

5)

12) RESEARCH IN PROGRESS **Briefly describe in 100 words or less.**

Characterization of protective efficacy of each vaccine vector completed for Seoul virus. Vectors are in the process of being modified to contain structual protein genes for all of the pathogenic members of the Hantavirus genus.

13) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH
Provide complete citation(s) including author(s), full name of journal, volume number, page number(s), year of publication.

(a) Publications in peer-reviewed journals:

Hooper, J.W., Kamrud, K.I., Elgh F., Custer, D., and Schmaljohn, C.S. 1999. DN Vaccination with Hantavirus M Segment Elicits Neutralizing Anti. ies and Protects against Seoul Virus Infectio. irology 255:269-278.

(b) Books or book chapters:

Schmaljohn, C.S., Kamrud, K.I., and Hooper, J.W. 1999. Recombinant DNA Vaccines for Hantaviruses. In: Factors in the Emergence and Control of Rodent-Borne Diseases (Saluzzo, J.F. and Dodet, B. eds). Elsevier, Paris (In press).

Kamrud, K.I. and Schmaljohn, C.S. 1999. Hantaviruses. In: Emerging and Reemerging Infectious Diseases. (Olive, M. eds). Eaton Publishing, Natick, MA. (Submitted).

(c) Manuscripts in preparation, manuscripts submitted:

Kamrud, K.I., Hooper, J.W., Elgh, F., and Schmaljohn, C.S. 1999. Comparison of Naked DNA, DNA-based Sindbis Replicon, and Packaged Sindbis Replicon Vectors Expressing Hantavirus Structural Genes in Hamsters. Virology (Submitted).

Ma M., Kersten, D.B., Kamrud, K.I., Wool-Lewis, R.J., Schmaljohn, C.S., and Gonzalez-Scarano, F. 1999. Pseudotyping of Murine Leukemia Virus with Glycoprotein from La Crosse Virus and Hantaan Virus. Virus Research (In press).

14) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete reference with author(s), title, abstract/proceeding citation, meeting name, location. Group into domestic and foreign.

4th International Conference on HFRS and Hantaviruses. 1998. K. Kamrud, T. Nelle, F. Elgh, L. VanderZanden, K. Anderson, and C. Schmaljohn "Evaluation of Naked DNA and Alphavirus Based Hantavirus Vaccines". Atlanta, Georgia.

Emergence and Control of Rodent-Borne Viral Diseases (Hantaviruses and Arenaviruses). 1998. K. Kamrud, J. Hooper, F. Elgh, and C. Schmaljohn "Packaged Sindbis Virus Replicons as Potential Hantavirus Vaccine Vectors". Les Pensieres, Veyrier-du-Lac, France.

NCI-FCRDC/Fort Detrick Spring Research Festival. 1999. K. Kamrud, J. Hooper, F. Elgh, and C. Schmaljohn "Comparison of the Immunogenicity and Protective Efficacy of Naked-DNA, DNA-based Sindbis Replicons, and Packaged Sindbis Replicon Vectors Expressing Seoul Virus Structural Genes in Hamsters". Frederick, Maryland.

15) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

16) NEW POSITION TITLE, ORGANIZATION and ADDRESS

Microbiologist, USAMRIID, Virology Division, Fort Detrick, Frederick, MD 21702

17) NEW POSITION PLANS **You may indicate more than one.**

- ☒ *Research -- National Government* (U.S. or Foreign)
- ☐ *Administration -- U.S. Govt.* (Fed., State, or Local)
- ☐ *Remain at Host Lab/Center*
- ☐ *College/University Professor*
- ☐ *Postdoctoral*
- ☐ *Uncertain*
- ☐ *Self-Employed*
- ☐ *Industry*
- ☐ *Other*

(Please provide name of Host Lab/Center.)

18) FORWARDING ADDRESS **(to which your tax statement will be mailed)**

6320 Towncrest Ct. Frederick, MD 21703

19) APPRAISAL OF THE ASSOCIATESHIP PROGRAM

Please evaluate each of the following on a scale of 1 (poor) to 10 (excellent):

10 a) Of what value was this experience to your career?

10 b) What is your evaluation of your experience in the laboratory?

10 c) What is your evaluation of your interaction with the NRC?

Please provide any additional comments on the usefulness of the Associateship Program to you, including suggestions for improvements.

The NRC Associateship program is excellent. I have only two comments. 1) Reimbursement of travel expenses was slow (ranging from 2-4 months) after travel was completed. Many times registration and accomodations costs had to be payed out 3 to 4 months in advance of the meeting, resulting in output of personal funds without compensation of up to half a year. A more streamlined method of reimbursement should be adopted to avoid such long delays in distribution of travel funds. 2) A clerical error in salary on the part of someone in the NRC in 1999 (or late 1998), resulted in the program having to collect back a portion of the salary over a 3 month period from all NRC associates at USAMRIID (perhaps other institutes as well?). Every effort

should be made NOT to repeat this fisc·l behavior. It reflects poorly on the program ? ' resulted in a great deal of financial difficulty over that period of time. I si .ly hope that the indivdual(s) responsible for .s mistake were reprimanded and made aware of the repercussions of their actions.

USPS Mailing Address	FAX Number	Express-Delivery Address
Associateship Programs [TJ 2114]	202 – 334 – 2759	Associateship Programs [Suite 2114]
NATIONAL RESEARCH COUNCIL	INTERNET	NATIONAL RESEARCH COUNCIL
2101 Constitution Avenue, NW	national-academies.org/rap	1000 Thomas Jefferson Street, NW
Washington, DC 20418		Washington, DC 20007

This shaded area is for the Associateship Programs Office use only. Rev: 5/1999

ID. # Copy To / Date Cost-Center #

Report Form

1) NAME: Guo Li
2) DATE: 9, 15, 1999
3) PROGRAM/AGENCY, LAB/CENTER, LOCATION: USAMRD, Bldg. 176, Brooks AFB, TX 78235.
4) DATE OF TENURE: 9, 15, 1996 – 9,15,1999.
5) NAME OF RESEARCH ADVISER: Harry Zwick.
6) IF YOU ARE ON LEAVE FROM A PROFESSIONAL POST, WILL YOU RETURN TO YOUR PREVIOUS EMPLOYER? No.
7) PROFESSIOINAL AWARDS RECEIVED, SOCIETY OFFICES HELD DURING TENERE: Non.
8) PROFESSIONAL TRAVEL DURING TENURE:
   (a) OSA annual meeting, October 12-17, 1997.
   (b) OSA annual meeting, October 4-9, 1998.
   (c) ARVO, MAY 10-15, 1998.
   (d) Photonics West, January 23-29, 1999.

9) SEMINARS OR LECTURE DELIVERED AT UNIVERSITY AND?OR INSTITUTES
10) TITLE OF RESEARCH PROPOSAL: imaging photoreceptors in the primate eye in vivo
11) SUMMARY OF RESEARCH DURING TENURE: Attached.
12) RESEARCH IN PROGRESS:

Characteristic diffractive optics of vertebrate eyes was exhibited based on the geometric characteristics of the eyes. We constructed the schematic eye model for the Checkered Garter snake. High order modes in snake photoreceptors were in vivo imaged using SLOs. The modal patterns, in normal versus laser damaged photoreceptor cells, appeared differently. Swollen photoreceptors exhibited laser injury to the membrane of photoreceptor cells. It is a very important laser retinal injury mechanism. We improved the ratio of signal to noise of PSFs by a confocal system. The asymmetrical properties of the PSFs referred to the optical axis of the human eye were revealed.

13) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

(1) "Wavequide Effects in Photoreceptors of the Living Snake Eyes" a journal paper in preparation.
(2) "On and Off Axis Point Spread Function Measurements Using Confocal Double Pass Method" a journal paper in preparation.
(3) G. Li, H. Zwick, B. Stuck, and J.Lund, "Retinal Image Quality in Small and Large Eye, " submitted to "Journal of biomedical optics" for publication.
(4) G. Li, H. Zwick, R. Elliott, A. Akers, S. Schuschereba, D. J. Lund, B. Stuck, and J. Loveday, "Schematic Eye Model and In Vivo Retinal Images in the Checkered Garter Snake Eye-(*Thamnophis m marcianus*), " submitted to "Journal of biomedical optics" for publication.

14) PRESENTATION AT SCIENTIFIC MEETINGS OR CONFERENCES

(5) H. Zwick, W. R. Elliott, G. Li, and B. E. Stuck, "An in Vivo Cellular Animal Model of Acute and Long Term Laser Induced Retinal Pathophysiology," NIH Image Workshop (1999)

(6) W. R. Elliott, H. Zwick, P. Edsall, G. Li, M. Reddix, "Oxidate Stress in Retinal photoreceptors after acute laser lesion: 2, 7, dichlorodihydrofluoresceindiacetate in small eye," Investigate Ophthalmology and Visual Science, 40 pp.955, 1999.

(7) G. Li, H. Zwick, J. Tribble, J. Ness, D. Lund, and M. Reddix "On and off Axis Confocal Double Pass Measurements of the Point Spread Function in the Human Eye," Proceedings of Ophthalmic Technologies IX, Vol. 3591, 351(1999).

(8) H. Zwick, R. Elliott, G. Li, A. Akers, P. Edsall, B. Stuck, "In-Vivo Imaging of Photoreceptor Structure and Laser Injury Pathophysiology in the Snake Eye," Proceedings of Ophthalmic Technologies IX, Vol. 3591, 368(1999).

(9) H. Zwick, R. Elliott, G. Li, P. Edsall, and B. Stuck, "Confocal Scanning Laser Ophthalmoscope of the Pathophysiological Damage Mechanism Induced by Acute Laser Exposure" 28th Neuroscience Annual Meeting, 343(1998).

(10) H. Zwick, W. R. Elliot, B. E. Stuck, D. J. Lund, S. T. Schuschereba and Guo Li, "In-vivo Laser Induced Photoreceptor Pathology and Vascular Physiology in Small Eye Animal Model," the proceeding of International Laser Safety Conference (1998).

(11) G. Li, H. Zwick, J. Ness, J. Tribble, J. Lund, and B. Stuck, "Evaluate the Retinal Image Quality in the Living Human Eye," 1998 OSA Annual Meeting, 72, 1998.

(12) H. Zwick, G. Li, B. E. Stuck, and R. Elliott, "The Role of Numerical Aperture in Occular Resolution of in Vivo Cellular Detail, " Laser in Modern Battlefield (1998)

(13) G. Li, H. Zwick, R. Elliott, A. Akers, B. Stuck, "Mode Structure Alterrations in Normal and Laser Exposed Vertebrate Photoreceptors in the Small High Numerical Aperture Eye of the Snake," presented in 1998 OSA Annual Meeting, 72 (1998).

(14) H. Zwick, G. Li, R. Elliott, B. E. Stuck, and P. Edsall, "In vivo Optically Enhanced CSLO Imaging of Laser Induced Photoreceptor Damage in the Snake Retina," Investigate Ophthalmology and Visual Science, 39 pp.589, 1998.

(15) G. Li, H. Zwick, A. Akers, R. Elliott, B. Stuck, J. Lund, and S. Schuschereba, "High Numerical Aperture and Small Eye Photoreceptors," 1997 OSA Annual Meeting, 68 (1997).

(16) H. Zwick, W. R. Elliot, D. J. Lund, Guo Li, S. T. Schuschereba and P. A. Edsall, "In Vivo Measurement of Acute Laser Cellular Alteration at the Photoreceptor and Vascular Layers in the Small Eye," Investigate Ophthalmology and Visual Science, 38, 405 (1997).

(17) H. Zwick, W. R. Elliott, D. J. Lund, Guo Li, S. T. Schuschereba and P. A. Edsall, "In Vivo Scanning Laser Ophthalmoscopic Characterization of Laser Induced Photoreceptor Retinal Damage and Induced Pathophysiological Alteration in Blood Cell Flow in Small Animal Model," International Symposium on Biomedical Optics, S. J. CA, February, 1997.

15) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATE RESEARCH: Non.

16) NEW POSITION TITLE, ORGNIZATION, ADDRESS: Non.

17) NEW POSITION PLANS: Uncertain.

18) FORWAREDING ADDRESS: 3601 Magic Dr. 202, San Antonio, TX 78229.

19) APPRAISAL OF THE ASSOCIATESHIP PROGRAM

a) Of what value was this experience to your career? Maybe excellent, maybe good, maybe..... too early to conclude.

b) What is your evaluation of your experience in the laboratory? 9

c) What is your evaluation with the NRC? 10.

report of NRC associateship research

1) Name of associate:

Chunyuan Luo Chunyuan Luo

2) Name of laboratory/center and location:

WRAIR
6825 16th Street, NW
Washington DC, 20307-5100

2) Date:

03/2/99

4) Dates of tenure:

Beginning at 03/12/96
Ending at 03/11/99

5) Title of Research Proposal:

Investigation of ligand modulation mechanism on reactivation of phosphoryl conjugates of acetylcholinesterase by bispyridinium oximes

6) Name of research adviser:

Dr. B.P. Doctor

7) If you are on a leave from a professional post, will you return to your previous employer?

Not decided

8) Professional society offices held during tenure

N/A

9) Professional travel during tenure

1. Sixth International Meeting on Cholinesterase
   La Jolla, CA
   March 20-24, 1998
2. Third International Meeting on Esterases reacting with Organophosphorus Compounds
   Dubrovnik, Croatia
   April 15-18, 1998
3. First Singapore International Symposium on Protection against Toxic Chemicals
   Singapor
   Dec. 2-4, 1998

10) Seminars or lectures delivered at universities and/or institutes

N/A

11) Summary of research during tenure

1. Quaternary ligand-induced acceleration of oxime reactivation of acetylcholinesterase-organophosphate conjugates occurs only with a number of oximes, such as TMB4, obidoxime, MMB4 and 2-PAM.
2. Oxime reactivation can be accelerated by quaternary liagnds of small-molecule, such as edrophonium and decamethonium.
3. Acceleration of reactivation always occurs when the reactivation kinetics does not follow the theoretical models, an indication of phosphoryl oxime re-inhibition of the reactivated enzyme during the reactivation.
4. Mutation of the mouse wild-type acetylcholinesterase in the position of 74 from D to N (elimination of the negative charge) decreases or eliminates ligand-induced acceleration of oxime reactivation.
5. Stable phosphoryl oximes formed both from the reaction mixture of MEPQ with oxime or reactivation media of MEPQ-enzyme conjugate were isolated and confirmed by 31P NMR.
6. The isolated phosphoryl oximes are more powerful inhibitors than the parent organophosphate for acetylcholinesterase with ki > 10^{-10} $M^{-1}.min^{-1}$. The above findings have established the relationship between ligand-induced acceleration of oxime reactivation and the phosphoryl oxime re-inhibition of the reactivated enzyme. They also suggest that serious problem may occur in the treatment of organophosphate toxicity with certain oximes, such as TMB4 and obidoxime, due to the generation of more powerful inhibitor, phosphoryl oxime.

will not fit on screen

12) Research in Progress

The associateship research began with the study of the ligand-induced acceleration of reactivation of OP (organophosphate)-inhibited acetylcholinesterase. During the three year's research period, the ligand-induced acceleration of reactivation was found to be only with certain oximes and OPs when abnormal reactivation kinetics was observed. The study using mutant enzyme D74N acetylcholinesterase substantiated that phosphoryl oxime was formed and re-inhibited the reactivated enzyme during reactivation. ^{31}P NMR study and HPLC isolation of the phosphoryl oximes finally enabled the characterization of phosphoryl oximes, the intermediates during reactivation. Relationship between the ligand-induced acceleration and re-inhibition of reactivated enzyme by phosphoryl oxime has been established and the role of phosphoryl oxime formation with nerve agents and some OP pesticides is now in study.

13) Publications and papers resulting from NRC associateship research

(1) Publications in peer-reviewed journals:

1. Chunyuan Luo, Yacov Ashani and Bhupendra P. Doctor. Acceleration of oxime-induced reactivation of organophosphate-inhibited fetal bovine serum acetylcholines-terase by mono- and bis-quaternary ligands. *Molecular Pharmacology* 1998, 53: 714-726.
2. Chunyuan Luo, Ashima Saxena, Yacov Ashani, Haim Leader, Zoran Radic, Palmer Taylor, and Bhupendra P. Doctor. Role of edrphonium in prevention of the re-inhibition of acetylcholinesterase by phosphorylated oxime. *Chemical-Biological Interactions* (1999), in Press.

(2) Books or book chapters:

1. Luo C, Ashani Y, Saxena A, Leader H, Maxwell DM, Taylor P, Doctor BP. Acceleration of oxime-induced reactivation of organophosphate-inhibited acetylcholinesterase by quaternary ligands. In "Structure and Function of Cholinesterases and Related Proteins", Doctor BP, Taylor P, Quinn DM, Rotundo RL, Gentry MK, eds. Proceedings of the Sixth International Meeting on Cholinesterases, 20-24 March 1998, La Jolla, CA., pp. 215-221.

(3) Manuscripts in preparation

1. Chunyuan Luo, Ashima Saxena, Miles Smith, Gregory Garcia, Zoran Radic, Palmer Taylor, and Bhupendra P. Doctor. Phosphoryl oxime inhibition of acetylcholinesterase that occurs upon oxime reactivation of the phosphorylated enzyme is prevented by edrophonium. Plan to submit to *Biochemistry*.

2. Debora Moorad, Chunyuan Luo, Shawn R. Feaster, Ashima Saxena, B. P. Doctor, and Gregory Garcia. Purification, characterization, and amino acid sequence of equine serum butyrylcholinesterase. Plan to submit to Biochimica et Biophysica Acta.

14) Presentations at scientific meetings or conferences

1. Acceleration of oxime-induced reactivation of organophosphate-acetylcholinesterase conjugate and ^{31}P NMR detection of phosphoryl oxime from the conjugate, presented at the "10th International Symposium on Cholinergic Mechanisms", Paris, Sep. 1-5, 1998
2. Acceleration of oxime-induced reactivation of OP-inhibited AChE by quaternary ligands, presented at the "6th International Meeting on Cholinesterase", San Diego, CA, Mar. 20-24, 1998

3. Role of edrophonium in prevention of the re-inhibition of acetylcholinesterase by phosphorylated oxime, presented at the "3rd International Meeting on Esterases Reacting with Organophosphorus Compounds", Dubnovnik, Croatia, Apr. 15-18, 1998

4. Acceleration of oxime-induced reactivation of acetylcholinesterase-organophosphate conjugate and ^{31}P NMR detection of phosphoryl oxime, invited to present at the 1st International Symposium on Protection against Toxic Chemicals, Dec. 1-4, 1998, Singapore

15) Patents or copyright applications resulting from NRC associateship research

N/A

16) Next position title, organization and address

Contracted Principal Investigator, WRAIR.

17) Next position status

Remain at Host lab (WRAIR)

18) Forwarding address

26 S. Old Glebe Rd., Apt. #2
Arlington, VA 22204

19) Appraisal of the associateship program

Of what value was this experience to your career? 8
What is your evaluation of your experience in the laboratory? 7
What is your evaluation of your interaction with the NRC? 8

REPORT: LUMLEY

1. December 30, 1998

2. Lucille A. Lumley

3. Walter Reed Army Inst. of Research, Washington, DC, 20307-5100

4. Tenure: Jan 2, 1996-Jan 2, 1999

5. Title: Neural mechanisms and pharmacological mechanisms of defeat.

6. Research Advisor: James L. Meyerhoff, M.D.

7. N/A

8. *Memberships*: Society for Neurosciences
American Association for the Advancement of Science
New York Academy of Sciences
WRAIR Human Relations Committee

9. *Professional travel*:
1996:
Attended the XII World Meeting of the International Society for Research on Aggression, Strasbourg, France, August 25-30, 1996.
Attended the Annual Meeting of the Society for Neuroscience, Washington, DC, November 16-21, 1996.

1997:
Attended inaugural meeting of Society for Behavioral Neuroendocrinology, Baltimore, MD, May 27-31, 1997.
Attended the meeting of the International Society for Psychoneuroendocrinology, San Francisco, CA, July 25-August 1, 1997.
Attended annual meeting of the Society for Neuroscience, New Orleans, LA, October 25-30, 1997.
Attended the International Workshop on the Behavioural Pharmacology of Anxiety and Depression. Bath, England, November 23-27, 1997

1998:
Attended meeting of the International Society for Psychoneuroendocrinology, Trier, Germany, August 1998.
Attended meeting sponsored by the New York Academy of Sciences, entitled "Advancing from the Ventral Striatum to the Extended Amygdala: Implications for Neuropsychiatry and Drug Abuse", Charlottesville, VA, October 18-21, 1998.
Attended annual meeting of Society for Neuroscience, Los Angeles, CA, November 6-12, 1998.
Attended meeting "Four Decades of Memory" honoring James L. McGaugh, Irvine, CA, November 6-7, 1998.

10. Seminars:
Division of Neuroscience, WRAIR, October 1997
Oral Presentation: Triers, Germany, ISPNE meeting, August 1998

11. Summary of Research During Tenure:
We developed a battery of behavioral tests and hormonal measures following acute social defeat (SD) in male DBA/2 mice in attempt to develop an animal model of acute stress disorder. We measured the time course of behavioral and hormonal changes following SD, and observed that defeated mice displayed prolonged inhibition of territorial urine marking, and prolonged avoidance of and defensive behaviors towards non-aggressive intruders. In addition, we tested the efficacy of select pharmacological agents in preventing or reversing effects of SD on exaggerated fear, defense, risk assessment, acoustic startle reflex, swim suppression, and territorial marking, in DBA/2 mice.

12. Research in Progress:
We are currently studying defeat-induced behavioral and hormonal changes following acute SD in male C57BL/6 mice, in order to examine strain differences in responses to defeat and in pharmacological efficacy in affecting aberrant defeat-induced behavioral changes. In addition to classical anxiolytics, we are testing some novel compounds for their potential as anxiolytics. We also plan to extend our social stress model to include tests of short term memory and to determine whether there is stress-induced neuropathology in defeated mice.

13. Publications and Papers Resulting from NRC:
a. Peer-reviewed publications:

Hebert MA, Evenson A, Lumley LA, and Meyerhoff JL (1998). Effects of acute social defeat on activity in the forced swim test: parametric studies in DBA/2 mice using a novel measurement device. Aggressive Behavior 24:257-269.

b. Published Abstracts:

Lumley LA, Hebert MA, Sipos ML, and Meyerhoff JL (1996). Evidence for long term behavioral effects of acute defeat. Neuroscience Abstracts, 22:461.

Hebert MA, Lumley LA, Evenson AR, and Meyerhoff JL (1996). Effects of acute social defeat on activity in the forced swim test: parametric studies in mice. Abstract, ISRA, p25.

Lumley LA, Charles RF, Charles RC, and Meyerhoff JL (1997). Naloxone partially blocked defeat-induced swim immobility in DBA/2 male mice. Abstract, Behav. Pharm. 8:654.

Sipos ML, Saviolakis GA, Charles, Charles, and Meyerhoff JL (1997). Effects of social defeat on defensive behaviors, urine marking, activity and acoustic startle reflex in male DBA/2 mice, and effects of DHEA on defeated mice, Abstracts, Soc. Behav. Neuroend.

Lumley LA, Saviolakis GA, Hebert MA, Charles RF, Charles RC, Pena BE, and Meyerhoff JL (1997). Defeat induced hormonal and behavioral changes in male DBA/2 mice: time course profile, Psychoneuroendocrinology, 22(S2), S177.

Lumley, Charles, Charles, and Meyerhoff (1997). Opposing effects of diazepam on fear responses in male DBA/2 mice tested in a modified resident-intruder test, Neuroscience Abstracts 23.

Saviolakis, Lumley, Charles, Charles, Sipos, Hebert, Pena, and Meyerhoff (1997). Time course profile of behavioral and hormonal changes following acute social defeat in male DBA/2 mice, Neuroscience Abstracts 23:1082.

Beaulieu, Smith, Hebert, Saviolakis, Lumley, Post, and Meyerhoff (1997). Effect of conditioned social defeat in mice on hypothalamic-pituitary-adrenal axis regulation, Neuroscience Abstracts 23:1354

Lumley LA, Saviolakis GA, Sipos ML, and Meyerhoff JL (1998). Effects of repeated social defeats on acoustic startle response and testosterone levels in male DBA/2 mice. Abstracts, International Society of Psychoneuroendocrinology, Trier, Germany, p. 20.

Lumley LA, Saviolakis GA, Charles RC, Charles RF, Smith IM, Meyerhoff JL (1998). Effects of diazepam and social defeat on risk assessment in a modified resident-intruder test, and on territorial urine marking in C57BL/6 mice, Neuroscience Abstracts 24.

Lumley LA, Charles RF, Charles RC, Morton DM, Booker CJ, Meyerhoff JL (1998). Diazepam administered 24 hours prior to a modified resident-intruder test induced exaggerated fear responses in male DBA/2 mice, Abstracts, Four Decades of Memory, a Festshrift honoring James McGaugh, UC Irvine.

c. Manuscripts submitted:

Lumley LA, Sipos ML, Charles RC, Charles RF, and Meyerhoff JL. Time course of effects of acute social stress on territorial urine marking and ultrasonic courtship vocalizations, in male DBA/2 mice. Submitted to Hormones and Behavior.

d. Manuscripts in preparation:

Lumley LA, Charles RF, Charles RC, Morton DM and Meyerhoff JL. Effects of diazepam on fear responses in male DBA/2 mice. (plan to submit to Psychopharmacology)

Lumley LA, Morton DM, Charles RF, Charles RC and Meyerhoff JL. Effects of diazepam and social defeat on risk assessment in a modified resident-intruder test, in male C57BL/6 mice.

Lumley LA, Saviolakis GA, Sipos ML, Charles RF, Charles RC, and Meyerhoff JL. Time course of defeat-induced behavioral and hormonal changes in male DBA/2 mice.

Lumley LA, Morton DM, Meyerhoff JL, and Slusher B, Effects of PMPA administered i.c.v. via osmotic minipumps on defeat-induced behavioral changes.

14. *Presentations at Scientific Meetings or Conferences*:

1996:

Presented Hebert MA, Lumley LA, Evenson AR, and Meyerhoff "Effects of acute social defeat on activity in the forced swim test: parametric studies in mice" at the International Society for Research on Aggression meeting, Strasbourg, France, August 1996.

Presented Lumley LA, Hebert MA, Sipos ML, and Meyerhoff JL "Evidence for long term behavioral effects of acute defeat" at the annual meeting of the Society for Neuroscience, Washington, DC, November 1996.

1997:

Presented Lumley, Sipos, Saviolakis, Charles, Charles, and Meyerhoff "Effects of social defeat on defensive behaviors, urine marking, activity and acoustic startle reflex in male DBA/2 mice, and effects of DHEA on defeated mice" at the Society for Behavioral Neuroendocrinology, Baltimore, MD.

Presented Lumley, Saviolakis, Hebert, Charles, Charles, Pena and Meyerhoff "Defeat induced hormonal and behavioral changes in male DBA/2 mice: time course profile", at the International Society of Psychoneuroendocrinology XVIIIth Congress, San Francisco, CA, July 25-August1.

Presented Lumley, Charles, Charles, and Meyerhoff "Opposing effects of diazepam on fear responses in male DBA/2 mice tested in a modified resident-intruder test" at the Society for Neuroscience meeting, New Orleans, LA, October 25-30.

Presented Saviolakis, Lumley, Charles, Charles, Sipos, Hebert, Pena, and Meyerhoff "Time course profile of behavioral and hormonal changes following acute social defeat in male DBA/2 mice" at the Society for Neuroscience meeting, New Orleans, LA, October 25-30.

Presented Lumley, Charles, Charles and Meyerhoff "Naloxone partially blocks defeat-induced swim immobility in DBA/2 male mice", at the International Workshop on the Behavioural Pharmacology of Anxiety and Depression, Bath, England, November 20-23.

1998:

Presented Lumley LA, Saviolakis GA, Sipos ML and Meyerhoff JL "Effects of repeated social defeat on acoustic startle response and testosterone levels in male DBA/2 mice" at the International Society for Psychoneuroendocrinology, 2-3 Aug 98, Trier, Germany.

Presented Lumley LA, Saviolakis GA, Charles RC, Charles RF, Smith IM, Meyerhoff JL "Effects of diazepam and social defeat on risk assessment in a modified resident-intruder test, and on territorial urine marking in C57BL/6 mice" at Society for Neurosciences, Abstracts 24.

14. Presentations at scientific meetings (continued)

Presented Lumley LA, Charles RF, Charles RC, Morton DM, Booker CJ, Meyerhoff JL "Diazepam administered 24 hours prior to a modified resident-intruder test induced exaggerated fear responses in male DBA/2 mice" at Four Decades of Memory, a Festshrift honoring James McGaugh, UC Irvine, 1998.

15. N/A

16. Future Position Title and Status:

National Government-Research
Remain at Host Agency- WRAIR
Sponsored by Jackson Foundation
Post-Doc

17. Forwarding address:

2445 Lyttonsville Rd., #702
Silver Spring, MD 20910

18) Appraisal of Associateship Programs:

I was pleased with the overall NRC associateship program. I particularly commend the NRC program for its maximal support of research, in that NRC fellows have minimal administrative duties, and are given much independence in their research. I also compliment the NRC staff, particularly Lisa Bevell and Judith Nyquist, Ph.D., both of whom responded promptly to questions and concerns.

My main criticism of the NRC program is the extensive delay in processing of travel expense reports. NRC fellows are required to submit forms immediately after travel, yet typically do not receive reimbursement for several months following submittal of these forms. A related criticism is that there should be a policy for the NRC to pay in advance for the registration fee to attend a meeting. Some meetings have exorbitant registration fees (over $700), which must be paid 6 months in advance. For the NRC fellow to have to wait 3 or 4 months *after* the close of the meeting (10 months post-payment out of pocket) to be reimbursed may prevent the fellow from attending an important meeting. However, I do praise the NRC in providing 80% of per diem travel funds prior to attending the meeting, as some agencies do not give any travel funds in advance.

A final criticism is of the failure of the NRC to provide tax advice. Since workman's compensation and health insurance fees are removed from the award, yet the fellow is not considered an employee, the appropriate way to file taxes is confusing to most NRC fellows, and the advice from the IRS is often inconsistent.

NATIONAL RESEARCH COUNCIL
ASSOCIATESHIP PROGRAMS
2101 CONSTITUTION AVE, NW, TJ 2114
WASHINGTON, DC 20418

REPORT

Your Final Report should follow this format and include the items listed below.

(1) DATE December 28, 1998

(2) **NAME (AND NRC ASSOCIATESHIP I.D. NUMBER IF KNOWN)** Dr. Da Ma

(3) NAME OF LABORATORY OR CENTER AND LOCATION Walter Reed Army Institute of Research
Washington, DC

(4) DATES OF TENURE January 28, 1997 - December 28, 1998

(5) TITLE OF RESEARCH PROPOSAL "A new approach to an old problem: High tech search for more effective mosquito repellents"

(6) NAME OF RESEARCH ADVISER Dr. Raj K. Gupta and Dr. Mustapha Debboun

(7) ARE YOU ON LEAVE FROM A PROFESSIONAL POST? No
If so, list position or title and address.

(8) PROFESSIONAL SOCIETY OFFICES HELD DURING TENURE

(9) PROFESSIONAL TRAVEL DURING TENURE Enclosed
List location(s) and date(s) of travel to scientific meetings. List foreign meetings separately.

(10) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Enclosed
List location(s) and date(s).

(11) SUMMARY OF RESEARCH DURING TENURE Enclosed
List significant findings in concise form (100 words or less). Please do NOT use Greek letters or mathematical signs and symbols.

(12) RESEARCH IN PROGRESS Enclosed

(13) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES Enclosed
Provide complete reference with author(s), title, abstract or proceeding citation, and meeting name and location.

(14) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Enclosed
Provide complete citation(s), including author(s), full name of journal, volume number, page number(s), and year of publication.
List separately:
(a) Publications in peer-reviewed journals;
(b) Books or book chapters; and
(c) Manuscripts in preparation, manuscripts submitted.

(15) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

(16) FUTURE POSITION AND ADDRESS AND/OR FORWARDING ADDRESS Enclosed

(17) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS Enclosed
Comment on your program and its usefulness to you. Suggest improvements in the overall Associateship Programs.

9) PROFESIONAL TRAVEL DURING TENURE

National meeting:

The 46th Annual Meeting of the American Society of Tropical Medicine and Hygiene, Orlando, Florida, **December 7-11, 1997.**

Foreign meeting:

The Third International Symposium on Biotechnology, Medicine and Pharmacy for Young Scientists, Beijing, China, **August 23-27, 1998.**

10) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTE

Walter Reed Army Institute of Research, Department of Entomology Seminar Series, Washington DC 20307-5100, **June 17, 1997**.

U. S. Department of Agriculture, Agriculture Research Service, Insect Chemical Ecology Laboratory Seminar Series, Beltsville, MD 20705-2350, **September 24, 1998**.

Walter Reed Army Institute of Research, Department of Entomology Seminar Series, Washington DC 20307-5100, **June 8, 1998**.

U. S. Department of Agriculture, Agriculture Research Service, Insect Chemical Ecology Laboratory Seminar Series, Beltsville, MD 20705-2350, **May 20, 1998**.

11) SUMMARY OF RESEARCH DURING TENURE

1. Established relationship between repellency and electronic properties of DEET analogs. Using quantum chemical methods, lowest energy conformations and molecular electronic properties were calculated for 31 amides. The calculated structural and electronic properties were then correlated with protection time to provide predictive discriminators of insect repellency and a better understanding the structure and repellency properties of these compounds.

2. Synthesized a group of chiral piperidine compounds. Starting materials were prepared through crystallization. Procedure of formulation of amide was modified. Crude compounds were purified by distillation or chromatography. Structure of each product was identified by IR, GC, GC-MS, and NMR. Studied the stereoelectronic features and calculated electronic properties of chiral forms.

3. Established relationship between electronic property of repellents and Juvenile hormone of insects.

4. Designed and synthesized 8 DEET–like and 9 DEPA-like compounds. Crude compounds were purified by distillation or chromatography. Structure of each product was identified by IR, GC, GC-MS, and NMR. Calculated electronic properties of those compounds using quantum chemical methods.

12) RESEARCH IN PROGRESS

In vitro testing and efficacy studies of all the chiral forms as well as DEET and DEPA analogs, which have been synthesized, are already underway.

13) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Da Ma, Apurba K. Bhattacharjee, Raj K. Gupta, and Jean M. Karle. "Predicting Mosquito Repellent Activity of DEET Analogs from Molecular Electronic Properties" *Am. J. Trop. Med. Hyg.*, 1998, in press.

Da Ma, Raj K. Gupta and Jerome A. Klun. "Optical Active Arthropod Repellents for Use in Bioassays Against Disease Vectors" *J. Med. Entomol.*, 1998, in preparation.

Da Ma, Raj K. Gupta and Jerome A. Klun. "NMR Analyses of the Optical Active Arthropod Repellents" *J. Med. Entomol.*, 1998, in preparation.

Apurba K. Bhattacharjee, Da Ma, Jean M. Karle and Raj K. Gupta. "Molecular Similarity Analysis between Insect Juvenile Hormone Mimics and N,N-diethyl-3-methylbenzamide (DEET) Analogs may Aid the Design of Novel Insect Repellents" *J. Med. Entomol.*, 1998, in preparation.

14) PRESENTATIONS AT SCIENTIFIC MEETINGS AND CONFERNCES

Da Ma, Apurba K. Bhattacharjee, Raj K. Gupta, and Jean M. Karle. Predicting Mosquito Repellent Activity of DEET Analogs from Molecular Electronic Properties. The 46th Annual Meeting of the American Society of Tropical Medicine and Hygiene, Orlando, Florida, **December 7-11, 1997**.

Da Ma, Apurba K. Bhattacharjee, Raj K. Gupta, and Jean M. Karle. Assessing Electronic Properties of Mosquito repellent Using Computer Modeling. The Third International Symposium on Biotechnology, Medicine and Pharmacy for Young Scientists, Beijing, China, **August 23-27, 1998**.

16) ADDRESS FOR MAILING TAX STATEMENT

Da Ma
2301 Ring St.
Rockville, MD 20851
Tel/Fax: 301-424-3007

17) APPRAISAL OF THE ASSOCIATESHIP PROGRAMS

The associateship programs conducted by the National Research Council provide great opportunities for researcher's contribution to a specified area of interest based on the need of the sponsoring laboratory.

I was very impressed with the leadership skills, scientific knowledge, and technical know-how of my advisor, Dr. Raj K. Gupta. I was given the full opportunity to exchange ideas, discuss techniques, and experiment new approaches. I am very thankful for Dr. Gupta's expert guidance throughout the program. I am also thankful for Dr. Mustapha Debboun's involvement, his understanding and support in the latter part of my associateship tenure. The joint efforts of these two people have made possible the successful completion of all the projects with which I began my NRC association.

My positive experience with NRC would not have been possible without the understanding and assistance of NRC's staff whose demonstrated professionalism deserves commendation. In particular, I would like to give thanks to Ms. Lisa E. Bevell for her assistance throughout my tenure.

Report
Research Associateship Programs

1. **Name**: **Dr. Sheila A. Peel**

2. **Date**: 08-02-99

3. **Program/Agency/Lab/Center/Location**: AMRDC/WRAIR/DIV ET/DEPART PARASITOLOGY

4. **Dates of tenure**: 08-01-96 to 07-31-99

5. **Research Advisor**: Maj. Rodger K. Martin

6. **Will you return to previous employer?** No

7. **Professional Adwards/Offices**: Appointed WHO technical advisor, Steering Committee on Drug Discovery Research, 1998-1999

8. **Professional travel**:
Domestic:
1. Molecular Parasitology Meeting, Woods Hole, MA, Sept. 15-19, 1996
45th Annual Meeting of American Society of Tropical Medicine, Baltimore, MD Dec 1-4, 1996
2. Malarial Genome Meeting, Baltimore, MD, Dec 5-6, 1996
3. 46th Annual Meeting of American Society of Tropical Medicine, Lake Buena Vista, FL, Dec 7-11, 1997
4. Consultant (non-paid), In vitro cultivation of Malarial Parasites, Dr. Dyann F. Wirth Harvard School of Public Health, Boston, MA, Jan 5-9, 1998
5. Malarial Genome Meeting, Rockville, MD, June 21-22, 1998
6. Molecular Parasitology Meeting, Woods Hole, MA, Sept. 13-17, 1998
7. Gordon Conference on Parasitism, Newport, RI, June 20-25, 1999
8. Molecular Parasitology Meeting, Woods Hole, MA, Sept. 13-17, 1999 (to be funded by WRAIR/DIV RETRO)

Foreign:
1. Gordon Conference on Malaria, Oxford UK, July 24-31, 1998
2. World Health Organization, Geneva, Switzerland Sept 6-9, 1998

9. **Seminars or Lectures**
Harvard School of Public Health, Harvard University, Boston, MA, Jan 7, 1998
World Health Organization, Geneva, Switzerland, Sept 7, 1998

10. **Title of Research Proposal:** Quinoline Resistance in *Plasmodium falciparum*

11. **Summary of Research:**
The function of the *pfmdr1* gene in quinoline drug resistance in the human malarial parasite, *Plasmodium falciparum,* has been extremely difficult to study in vitro derived parasite lines and field isolates due to the contribution of background genetics. Expression studies overproducing the *pfmdr1*gene product, Pgh1, in an unaltered genetic background represented an approach to analyze this protein's potential role in transport processes, mediation of resistance phenotypes, and pharmacological chemosensitization. The aim of this research was to develop a heterologous expression system for the *pfmdr1* gene, *Plasmodium falciparum* using infectious cDNA replicon systems.
(1) Experiments were designed to express *pfmdr1* in an infectious cDNA Alpha virus, Venezuelan Equine Encephalitis (VEE) replicons.**(a)** Polymerase chain reaction protocols for amplification of full-length *pfmdr1*, (4,354 nucleotides of an 82% A/T-rich sequence), and gyrase protocols for efficient subcloning of full length gene into the Venezuelan Equine Encephalitis shuttle vector were developed. **(b)** Studies identified T7 RNA Polymerase termination sites in *pfmdr1*preventing read-through by T7 Polymerase, thus aborting transcription. Site directed mutagenesis was performed to alter T7 termination sites in overlapping gene fragments of *pfmdr1*. ABI automated sequencing of overlapping modified fragments ensured sequence fidelity. RNA transcription run-off studies

determined efficient read-through by T7 polymerase. (c) Modified fragments were ligated, sequence fidelity at ligation junctions confirmed by automated sequencing analysis, then the full length pfmdr1 gene was subcloned into VEE shuttle vector, SH-1 (obtained from Dr. Robert Johnston, University of North Carolina at Chapel Hill). Full-length *pfmdr1* constructs subcloned into shuttle vector were highly unstable resulting in recombination rearrangement in replicons isolated from over 20 bacterial strains used in recombinant research. (2) A novel non-cytopathic *Sndbis* viral replicon, pSINrep19, a second generation Alpha virus heterologous gene expression system, based on the VEE replicon system, was then obtained from Dr. Charles Rice, University of Washington at St Louis. This construct was more robust than the first generation VEE replicon system, allowed larger inserts than VEE, did not require the use of a shuttle vector, and allowed persistent heterologous expression of genes with minimal perturbation to host cellular processes. (a) Modifications to the pSINrep19 multicloning site, and continued screening of bacterial mutants failed to yeild stable constructs of full-length modified *pfmdr1*. (b) Analysis of additional *rec*$^-$ bacterial strains under development by Stratagene, Inc. also yielded rearranged replicons. (c) Passage of replicons containing inserts of more than 2000 nuleotides of 82% A/T-rich sequence appear to induce a recombination repair activity bacteria yielding highly rearranged replicons. To date, full-length recombinant construct of the modified *pfmdr1* product has not been isolated. (d) Development of a high-level expression system for *Plasmodium falciparum* will likely depend upon strategies designed to circumvent passage of large recombinant constructs through bacteria.

(3) Concurrent with efforts to develop an expression system for falciparum malaria, efforts were directed toward establishing a stable gene transfection system for the laboratory. Transgene transfection of *P. falciparum* requires the movement of DNA across four membranes (1 erythrocyte, 3 parasite) prior to chromosomal integration events. (a) Transient transfection studies were conducted with a luciferase reporter construct, pHLH-1, (obtained from Dr. Dyann Wirth, Harvard) using a BTX Cell Manipulator 600 to determine plasmid concentration, voltage, number of pulses, and pulse length. (b) A Dihydrofolate reductase (DHFR) inhibitor (pyrimethamine) plasmid construct, PDT.Dd2, (obtained from Dr. Thomas Wellems, NIH) was used to develop stable transfection protocols for DHFR sensitive parasite clones. Results indicated that 10^7 parasites transfected with 65 µg plasmid pDT.Dd2 at 500 volts, for a total pulse interval of 9-12 msec (4 pulses at 3 msec per pulse) yielded stable transformants. (c) Protocols to maintain stringent selection and drive integration events at higher efficiency were developed. Briefly, parasites were maintained without selection drug for 48 hr, media was removed, then the parasitized erythrocyte pellet was resuspended in medium containing the IC90 level of parasite line to the selection drug. Parasites were maintained in this medium for 4 weeks, then transferred to the approximate IC_{50} of parasite line to selection drug. (d) Plasmid rescue experiments, and Southern blot analysis confirmed stable integration events. (e) Transfection efficiency was determined to be quite low, $1:10^7$

12. Research in Progress: As the *Plasmodium falciparum* genome project moves rapidly toward completion, microarray technology presents a powerful approach to conduct simultaneous genome-wide surveys of the estimated 5000-6000 *P. falciparum* genes. This technology provides a unique opportunity to gain a detailed understanding of growth, development, differentiation, and pathogenic processes of the parasite as well as a means to accelerate drug discovery efforts. DNA print prototype microarrays of *P. falciparum* using expression sequence tag, and open reading frame PCR products are currently being developed. DNA targets in the form PCR products are arrayed onto glass microscope slides using a highspeed robotic arm. RNA from parasite clones labeled with fluorescent dyes by reverse transcription is hybridized to the arrayed clones. A scanning confocal microscope is used to measure emission spectra of incorporated targets excited by Green (532 nm) and Red (632) lasers. Expression profiles are generated by analyses of clone identifier, signal intensity, intensity ratios, normalization constants, and confidence intervals.

13. Publications and Papers:

Peer-reviewed Journals:

1. Episodic evolution mediates interspecies transfer of murine coronovirus.1997. *J. Virol.* 1:1946-1955
2. Selection and characterization of chloropromazine resistant lines of *Plasmodium falciparum*, submitted, *Antimicrob. Agents Chemother,*July, 1999
3. Stable Square Wave Transfection of *Plasmodium falciparum,* submitted, July 31, 1999, *Mol. Microbiology*
4. Isolation of isogenic parasite lines using a semi-automated microdilution technique, in process to be submitted to *Exp. Parasiol.*, Aug 1999

Reviews:
1. ABC transporter genes of *Plasmodium falciparum*, invited review for *Drug Resistance Updates* (in process)

14. Presentations Scientific Meetings/Conferences:
1. Peel, SA, Yount, BL, Bell, CA, and Baric, RS. Development of an in vitro model to study pharmacological chemosensitization in *Plasmodium falciparum*.46th Annual Meeting of American Society of Tropical Medicine, Lake Buena Vista, FL, Dec 7-11, 1997
2. Peel, SA., O'Neil, M., Kesler, J., Martin, R.K., and D. Kyle. Stable square-wave transfection of *P. falciparum*. Molecular Parasitology Meeting, Woods Hole, MA, Sept. 13-17, 1998
3. Peel, SA., O'Neil, M., Kesler, J., Martin, R.K., and D. Kyle. Novel linear square-wave transfection technique for*Plasmodium falciparum*. Gordon Conference on Parasitism, Newport, RI, June 20-25, 1999
4. Peel, SA., Ben Mamoun, C., Goldberg, D., and R.K. Martin, Development of Prototype cDNA Print Microarrays for *Plasmodium falciparum.* Molecular Parasitology Meeting, Woods Hole, MA, Sept. 13-17, 1999 (to be funded by WRAIR/DIV)

15. Patent or Copyright Applications: None

16. New Position Title, Organization, Address:
Microbiologist
Department Molecular Diagnostics/Pathogenesis
Division of Retrovirology
WRAIR
1600 East Gude Dr.
Rockville, MD 20851

17. New Position Plans: Research- National Government

18. Forwarding Address:
Dr. Sheila A. Peel
1121 Clagget Dr.
Rockville, MD 20850

19. Appraisal of Associateship Program (evulation 1-10 scale)
Of what value was this experience to your career? **7**
What is your evaluation of your experience in the laboratory? **7**
What is your evaluation of your interaction with the NRC? **10**

Report
Research Associateship Programs

1. **Name**: **Dr. Sheila A. Peel**

2. **Date**: 08-02-99

3. **Program/Agency/Lab/Center/Location**: AMRDC/WRAIR/DIV ET/DEPART PARASITOLOGY

4. **Dates of tenure**: 08-01-96 to 07-31-99

5. **Research Advisor**: Maj. Rodger K. Martin

6. **Will you return to previous employer?** No

7. **Professional Adwards/Offices**: Appointed WHO technical advisor, Steering Committee on Drug Discovery Research, 1998-1999

8. **Professional travel**:
Domestic:
1. Molecular Parasitology Meeting, Woods Hole, MA, Sept. 15-19, 1996
45th Annual Meeting of American Society of Tropical Medicine, Baltimore, MD Dec 1-4, 1996
2. Malarial Genome Meeting, Baltimore, MD, Dec 5-6, 1996
3. 46th Annual Meeting of American Society of Tropical Medicine, Lake Buena Vista, FL, Dec 7-11, 1997
4. Consultant (non-paid), In vitro cultivation of Malarial Parasites, Dr. Dyann F. Wirth Harvard School of Public Health, Boston, MA, Jan 5-9, 1998
5. Malarial Genome Meeting, Rockville, MD, June 21-22, 1998
6. Molecular Parasitology Meeting, Woods Hole, MA, Sept. 13-17, 1998
7. Gordon Conference on Parasitism, Newport, RI, June 20-25, 1999
8. Molecular Parasitology Meeting, Woods Hole, MA, Sept. 13-17, 1999 (to be funded by WRAIR/DIV RETRO)

Foreign:
1. Gordon Conference on Malaria, Oxford UK, July 24-31, 1998
2. World Health Organization, Geneva, Switzerland Sept 6-9, 1998

9. **Seminars or Lectures**
Harvard School of Public Health, Harvard University, Boston, MA, Jan 7, 1998
World Health Organization, Geneva, Switzerland, Sept 7, 1998

10. **Title of Research Proposal:** Quinoline Resistance in *Plasmodium falciparum*

11. **Summary of Research:**
The function of the *pfmdr1* gene in quinoline drug resistance in the human malarial parasite, *Plasmodium falciparum,* has been extremely difficult to study in vitro derived parasite lines and field isolates due to the contribution of background genetics. Expression studies overproducing the *pfmdr1* gene product, Pgh1, in an unaltered genetic background represented an approach to analyze this protein's potential role in transport processes, mediation of resistance phenotypes, and pharmacological chemosensitization. The aim of this research was to develop a heterologous expression system for the *pfmdr1* gene, *Plasmodium falciparum* using infectious cDNA replicon systems.
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determined efficient read-through by T7 polymerase. (c) Modified fragments were ligated, sequence fidelity at ligation junctions confirmed by automated sequencing analysis, then the full length pfmdr1 gene was subcloned into VEE shuttle vector, SH-1 (obtained from Dr. Robert Johnston, University of North Carolina at Chapel Hill). Full-length *pfmdr1* constructs subcloned into shuttle vector were highly unstable resulting in recombination rearrangement in replicons isolated from over 20 bacterial strains used in recombinant research. **(2)** A novel non-cytopathic *Sndbis* viral replicon, pSINrep19, a second generation Alpha virus heterologous gene expression system, based on the VEE replicon system, was then obtained from Dr. Charles Rice, University of Washington at St Louis. This construct was more robust than the first generation VEE replicon system, allowed larger inserts than VEE, did not require the use of a shuttle vector, and allowed persistent heterologous expression of genes with minimal perturbation to host cellular processes. **(a)** Modifications to the pSINrep19 multicloning site, and continued screening of bacterial mutants failed to yeild stable constructs of full-length modified *pfmdr1*. **(b)** Analysis of additional *rec*$^-$ bacterial strains under development by Stratagene, Inc. also yielded rearranged replicons. **(c)** Passage of replicons containing inserts of more than 2000 nuleotides of 82% A/T-rich sequence appear to induce a recombination repair activity bacteria yielding highly rearranged replicons. To date, full-length recombinant construct of the modified *pfmdr1* product has not been isolated. **(d)** Development of a high-level expression system for *Plasmodium falciparum* will likely depend upon strategies designed to circumvent passage of large recombinant constructs through bacteria.

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13. Publications and Papers:

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15. Patent or Copyright Applications: None

16. New Position Title, Organization, Address:
Microbiologist
Department Molecular Diagnostics/Pathogenesis
Division of Retrovirology
WRAIR
1600 East Gude Dr.
Rockville, MD 20851

17. New Position Plans: Research- National Government

18. Forwarding Address:
Dr. Sheila A. Peel
1121 Clagget Dr.
Rockville, MD 20850

19. Appraisal of Associateship Program (evulation 1-10 scale)
Of what value was this experience to your career? **7**
What is your evaluation of your experience in the laboratory? **7**
What is your evaluation of your interaction with the NRC? **10**

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

RESEARCH ASSOCIATESHIP PROGRAMS

If you have downloaded this, you may print out and enter the information manually, or you may enter the information electronically, then return as an e-mail attachment.

1) NAME

James B. Phillips

2) DATE

June 17, 1999

3) *Program / Agency* *or enter abbreviation*	*Lab / Center*	*Location*
AMRMC	**WRAIR**	**Washinton, D.C. 20307-5100**

4) DATES OF TENURE

October 6, 1997 -- to – July 16, 1999

5) NAME OF RESEARCH ADVISER

Frank C. Tortella

6) IF YOU ARE ON LEAVE FROM A PROFESSIONAL POST, WILL YOU RETURN TO YOUR PREVIOUS EMPLOYER?

☐ Yes ☒ No

7) PROFESSIONAL AWARDS RECEIVED, SOCIETY OFFICES HELD DURING TENURE

XIIIth International Congress of Pharmacology Young Scientist Award (Travel to attend XIIIth International Congress of Pharmacology in Munich, Germany, July 1998).

8) PROFESSIONAL TRAVEL DURING TENURE **List location(s) and date(s) of travel to scientific meetings; group into domestic and foreign.**

Domestic:
New Orleans, LA, October 25-30, 1997
Los Angeles, CA, November 7-12, 1998
Washington, DC, April 17-21, 1999
Foreign:
Munich, Germany, July 26-31, 1998 (not funded by NRC)

9) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES **List location(s) and date(s).**

Walter Reed Army Institute of Research, February 10, 1999.

10) TITLE OF RESEARCH PROPOSAL

The role of the ubiquitin-proteasome pathway in secondary injury of neural trauma.

11) SUMMARY OF RESEARCH DURING TENURE **Itemize significant findings in concise form. Utilize concepts and key words.**

1) PS519 is a small molecule inhibitor of the 26S proteasome.

2) PS519 significantly reduced ischemic brain injury in a rat model of stroke.

3) PS519 treatment significantly improved brain EEG activity in injured animals.

4) PS519 illicited significant improvements in neurological function in injured rat

5) Brain leukocyte infiltration was significantly reduced in injured rats w/ PS519.

12) RESEARCH IN PROGRESS **Briefly describe in 100 words or less.**

Drug-induced physiology (MABP, HR, blood gases) studies in injured rats.

13) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citation(s) including author(s), full name of journal, volume number, page number(s), year of publication.

(a) Publications in peer-reviewed journals:

(b) Books or book chapters:

(c) Manuscripts in preparation, manuscripts submitted:

Phillips, James B., Williams, Anthony J., Elliott, Peter J., Adams, Julian and Tortella, Frank C., The proteasome inhibitor, PS519, reduces infarction in a rat model of cerebral ischemia. Proc. Natl. Acad. Sci. USA, July 1999, Submitted

14) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete reference with author(s), title, abstract/proceeding citation, meeting name, location. Group into domestic and foreign.

Domestic:

Williams AJ, JB Phillips, JC Hunter and FC Tortella, RS100642, A novel sodium channel blocker, reduces infarct volumen and improves funtional recovery folling MCAo and reperfusion in rats. Soc Neurosci Abst, (1999), In Press. Society for Neuroscience Annual Meeting in Miami, FL.

Phillips JB, AJ Williams, PJ Elliott and FC Tortella, A novel proteasome inhibitor, PS519, shows neuroprotective efficacy in a rat model of transient focal ischemia. The FASEB Journal, 13 (1999) A1099. Experimental Biology '99 in Washington, DC.

Phillips JB, AJ Williams, JR Dave, PJ Elliott and FC Tortella, PS-519, a novel proteasome inhibitor, reduces infarction in a rat model of ischemia/reperfusion brain injury. Soc Neurosci Abst, 24 (1998) 215. Society for Neuroscience Annual Meeting in Los Angeles, CA.

Williams AJ, J Long, JB Phillips, JR Dave, Y Lin, P Cui, T McCabe, J Nielsen, R Layer, LM Zhou and FC Tortella, Conantokin-G decreases hypoxic/hypoglycemic (H/H) injury in cultured rat neurons and decreases infarction in a rat model of focal cerebral ischemia. Soc Neurosci Abst, 24 (1998) 978. Society for Neuroscience Annual Meeting in Los Angeles, CA.

Foreign:

Phillips JB and BM Cox, Dopamine D1-receptor stimulation of GABA release from fetal rat primary striatal cultures. Naunyn-Schmied Arch Pharmacol, 358:1 (1998) R149. XIIIth International Congress of Pharmacology in Munich, Germany.

15) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

16) NEW POSITION TITLE, ORGANIZATION and ADDRESS

Staff Scientist, Henry M. Jackson Foundation
Uganda Virus Research Institute
P.O. Box 49
Entebbe, Uganda

17) NEW POSITION PLANS **You may indicate more than one.**

- ☒ *Research -- National Government* (U.S. or Foreign)
- ☒ *Administration -- U.S. Govt.* (Fed., State, or Local)
- ☐ *Remain at Host Lab/Center*
- ☐ *College/University Professor*
- ☐ *Postdoctoral*
- ☐ *Uncertain*
- ☐ *Self-Employed*
- ☐ *Industry*
- ☒ *Other*

(Please provide name of Host Lab/Center.) **WRAIR & HMJF**

18) FORWARDING ADDRESS **(to which your tax statement will be mailed)**

Effective August 20, 1999:
James B. Phillips c/o Rebecca Rohrer
USAID/Kampala-Uganda
US State Department
Washington, DC 20521-2190

19) APPRAISAL OF THE ASSOCIATESHIP PROGRAM

Please evaluate each of the following on a scale of 1 (poor) to 10 (excellent):

10 a) Of what value was this experience to your career?

9 b) What is your evaluation of your experience in the laboratory?

8 c) What is your evaluation of your interaction with the NRC?

Please provide any additional comments on the usefulness of the Associateship Program to you, including suggestions for improvements.

The program office is very efficient in offering assistance and answering administrative questions, however travel reimbursement usually required an excessive amount of time.

Dr. Avraham Shitzer
Department of Mechanical Engineering
Technion, Israel Institute of Technology
Haifa, Israel 32000

National Research council
Associateship Programs
2101 Constitution Ave., NW TJ 2114
Washington DC 80418
U.S.A.

Report

1) Date: Oct. 26, 1997
2) Laboratory: US Army Institute of Environmental Medicine, Natick, MA.
4) Dates of tenure: Aug. 12, 1996 - Sept. 29, 1997
5) Tittle of research proposal:
   Development of mathematical algorithms for simultaneous finger-tip temperatures and blood perfusion rates during cold stress.
6) Research adviser: Dr. Richard R. Gonzalez
7) On leave from the Technion, Israel Institute of Technology, Haifa, ISRAEL 32000, James H. Belfer, Professor of Mechanical Engineering.
8) Professional society offices held: none
9) Professional travel:
   (a) National Scientific meetings:
      1) International Mechanical Engineering Congress, Atlanta, GA. 19 - 21.11.96
      2) Experimental Biology '97, New Orleans, LA. 7 - 9.4.97
      3) Future of Biotechnology, Allerton, IL 18 - 21.4.97

   (b) Foreign Scientific meetings:
      1) The 7th International conference on Environmental Ergonomics, Jerusalem, Israel. 27.10 - 1.11.96

(e) A. Shitzer, Estimating endurance times by modeling the biothermal behavior of cold-stressed fingers. Allerton Workshop on the Future of Biothermal Engineering Allerton, IL 4/1997.

14) Publications:

(a) Peer-reviewed journals:

(1) A. Shitzer, L.A. Stroschein, M.W. Sharp, R.R. Gonzalez and K.B. Pandolf, Simultaneous measurements of finger-tip temperatures and blood perfusion rates in a cold environment. Journal of Thermal Biology, 1997 (in press).

(2) A. Shitzer, S. Bellomo, L.A. Stroschein, R.R. Gonzalez and K.B. Pandolf, Simulation of a cold-stressed finger including the effects of wind, glove and cold-induced vasodilatation. ASME Journal of Biomechanical Engineering, 1998 (in press).

(b) Book Chapter:

A. Shitzer, S. Bellomo, L.A. Stroschein, R.R. Gonzalez and K.B. Pandolf, Numerical model of the thermal behavior of an extremity in a cold environment including counter-current heat exchange between the blood vessels (tentative title). Solicited by Gordon and Breach International Series in "Engineering, Technology and Applied Science" volume on "Computer Techniques in Medical and Biotechnology Systems." 1998/9

(c) Manuscripts submitted:

(1) A. Shitzer, T.L. Endrusick, L.A. Stroschein, R.F. Wallace and R.R. Gonzalez, Characterization of a three-phase response in cold-stressed fingers. Submitted to the European Journal of Applied Physiology and Occupational Physiology.

(2) A. Shitzer, T.L. Endrusick, L.A. Stroschein, R.F. Wallace and R.R. Gonzalez, Heat loss efficiency economy of fingers during cold induced vasodilatation. Submitted to the Journal of Applied Physiology.

REPORT

Dec 11, 1998

Anjali Yadava

3) Walter Reed Army Institute of Research, Washington D.C.

4) Jan 2, 1996 – Dec 31, 1998

5) Title: **Cloning, characterization and immunogenicity of Sequestrin, a cytoadherent protein of malaria.**

6) Advisor: LTC. C.F. Ockenhouse

7) No

8) None

9) Professional Travel:

Hyderabad, India, August 18-22, 1997 to present paper at the 2nd Global Meet on Parasitic Diseases.

New Delhi, India, Nov 1-6, 1998 to present paper at the Xth International Immunology Congress.

10) None

11) Summary of Research:

Plasmodium falciparum is a serious threat to people residing in, or traveling to, endemic areas. The most severe complication is caused by the sequestration of mature parasites to the vascular endothelium of the brain. In an effort to prevent or reverse this binding we are looking at a parasite ligand, sequestrin, as a vaccine candidate. During my tenure as an NRC candidate, I have cloned and expressed several sequestrin constructs and tested their immunogenicity in mice, rats, rabbits and monkeys. I have also mapped the minimal CD36 binding domain of sequestrin and the putative amino acids involved in receptor interaction in an attempt to better understand the receptor-ligand interaction which would aid in designing better vaccines.

12) Research in Progress:

We are in the process of optimizing the best adjuvant/route of immunization in an attempt to elicit the best blocking antibodies. I am also continuing to look for sequestrin homologues in other Plasmodia.

13) None so far (anticipate publications within this year).

14) Presentations in Scientific Meetings:

A. Yadava. M.Brown, T. Scharton-Kersten, G. Glenn, DG Heppner & CF Ockenhouse. Development and evaluation of sequestrin, a CD36-binding ligand of P.falciparum as an anti-cytoadherence vaccine. Xth International Congress of Immunology, Nov 1-6, New Delhi, India.

A Yadava & CF Ockenhouse. Identification of minimal CD36-binding domain within Sequestrin, a P.falciparum protein involved in cytoadherence. 2nd Global Meet on Parasitic Diseases, August 18-22, 1997, Hyderabad, India.

A Yadava, P Duffy, J Berzofsky, S Kumar and CF Ockenhouse. Immunogenicity of Sequestrin, a cytoadherence molecule of P.facliparum in congenic mice. 45th Annual Meeting of ASTMH, Baltimore, MD. December Dec 1-5, 1996

15) Patent or Copyright: None

16) Future Position Title and Status:
Continue at WRAIR as Scientist

17) Forwarding Address: Same as before
(11801 Rockville Pike, #1601, Rockville, MD 20852)

18) The Associate Program helped me to spend some valuable time at a good research lab and gave me an opportunity to develop my interests further.

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

Associateship Programs

REPORT FORM

If you have downlo ed this form, enter the information electronically.
Return this form directly the NRC as an e-mail attachment or print out and mail.

1) NAME
DANIEL S. MORAN

2) DATE July 30, 1999

3) *Program / Agency* *Lab / Center* *Location*
or enter abbreviation USARIEM NATICK, MA
click on prgm/agnc

4) DATES OF TENURE
7-97 -- to - 7-99

5) NAME OF RESEARCH ADVISER
DR. KENT B. PANDOLF

6) IF YOU ARE ON LEAVE FROM A PROFESSIONAL POST, WILL YOU RETURN TO YOUR PREVIOUS EMPLOYER?
☒ Yes ☐ No

7) PROFESSIONAL AWARDS RECEIVED, SOCIETY OFFICES HELD DURING TENURE

8) PROFESSIONAL TRAVEL DURING TENURE **List location(s) and date(s) of travel to scientific meetings; group into domestic and foreign.**
SEE attached

9) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES **List location(s) and date(s).**
SEE attached

10) TITLE OF RESEARCH PROPOSAL
Physiological strain Indexes

11) SUMMARY OF RESEARCH DURING TENURE **Itemize significant findings in concise form (25 words/250 characters.)**
Utilize concepts and key words.
1) Developed New physiological strain index (PSI)
2) Developed New cold strain index (CSI)
3) In progress: A wrist size automatic physiological and environmenta
4) monitor (WAPEM)
5)

12) RESEARCH IN PROGRESS **Briefly describe in 100 words or less.**

13) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH
Provide complete citation(s) including author(s), full name of journal, volume number, page number(s), year of publication.

(a) Publications in peer-reviewed journals:
SEE Attached

(b) Books or book chapters:
SEE attached

(c) Manuscripts in preparation, manuscripts submitted:

SEE Attached

14) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete reference with author(s), title, abstract/proceeding citation, meeting name, location. Group into domestic and foreign.

SEE Attached

15) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide titles and dates of application.

16) NEW POSITION TITLE, ORGANIZATION, ADDRESS

Head Military Physiology Unit, Medical Corps, I.D.F.

17) NEW POSITION PLANS **You may indicate more than one.**

- ☐ *Research -- National Government* (U.S. or Foreign)
- ☐ *Administration -- U.S. Govt.* (Fed., State, or Local)
- ☐ *Remain at Host Lab/Center*
  Abbreviate Host Lab/Center: _____
- ☐ *College/University Professor*
- ☐ *Postdoctoral*
- ☐ *Uncertain*
- ☐ *Self-Employed*
- ☐ *Industry*
- ☐ *Other*
  Please specify: _____

18) FORWARDING ADDRESS **(to which your tax statement will be mailed)**

HELLER INSTITUTE OF MEDICAL RESEARCH, SHEBA MEDICAL CENTER
TEL-HASHOMER, 52621 ISRAEL

19) APPRAISAL OF THE ASSOCIATESHIP PROGRAM

Please evaluate each of the following on a scale of 1 (poor) to 10 (excellent):

10 a) Of what value was this experience to your career?

9 b) What is your evaluation of your experience in the laboratory?

9 c) What is your evaluation of your interaction with the NRC?

Please provide any additional comments on the usefulness of the Associateship Program to you, including suggestions for improvements.

USPS Mailing Address
Associateship Programs [TJ 2114]
NATIONAL RESEARCH COUNCIL
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Washington, DC 20418

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INTERNET
national-academies.org/rap

Express-Delivery Address
Associateship Programs [Suite 2114]
NATIONAL RESEARCH COUNCIL
1000 Thomas Jefferson Street, NW
Washington, DC 20007

This shaded area is for the Associateship Programs Office use only. Rev: 5/1999

ID # Copy To / Date Cost-Center #

Daniel S. Moran

PUBLICATIONS (July 1997- July 1999)

a. Full length papers

Moran D. S., Shitzer A., and Pandolf K. B.: A physiological strain index to evaluate heat stress. *Am. J. Physiol.* 275 (Regulatory Integrative Comp. Physiol. 44): R129-R134, 1998.

Moran D. S., Montain S. J., and Pandolf K. B.: Evaluation of different levels of hydration using a new physiological strain index (PSI). *Am. J. Physiol.* 275 (Regulatory Integrative Comp. Physiol. 44): R854-R860, 1998.

Moran D. S., M. Horowitz, U. Meiri, A. Laor, and K. B. Pandolf: Thephysiological strain index applied for heat-stressed rats. *J. Appl. Physiol.* 86(3): 895-901, 1999).

Moran D. S., and Pandolf K. B.: Wet Bulb Globe Temperature (WBGT)- to what extent is GT essential? *Aviat. Space Environ. Med.* 70(5): 480-484, 1999.

Moran D.S., Shapiro Y., Laor A., Izraeli S., and Pandolf K. B.: Can gender differences during exercise-heat stress be assessed by the physiological strain index? *Am. J. Physiol.* 45: R1798-R1804, 1999.

Moran D. S., Castellani J. W., O'Brien C., Young A., and Pandolf K. B.: A cold strain index (CSI) to evaluate physiological strain during cold exposure. *Am. J. Physiol.* 46:Rxxx-Rxxx, 1999.

Moran D. S., Kenney W. L., Pierzga J. M., and Pandolf . K. B.: Assessing different age groups during exercise-heat exposure by the physiological strain index (PSI). *J. Appl. Physiol.* (in review).

b. Books Chapters

Gaffin S. and Moran D. S.: Pathophysiology of heat-related illnesses. In: *Wilderness Medicine: management of wilderness and environmental emergencies,* Auerbach P.S. (ed.), Mosby, St. Louis, chap. 10, 1999.

Moran D. S., and Gaffin S.: Clinical management of heat-related illnesses. In: *Wilderness Medicine: management of wilderness and environmental emergencies,* Auerbach P.S. (ed.), Mosby, St. Louis, chap. 11, 1999.

c. Technical Reports

Moran D. S. and Pandolf K. B.: A physiological strain index (PSI) to evaluate heat stress. USARIEM Technical Report T99-xx, July 1999 (in preparation).

Encl

d. Proceedings and mini-papers

Moran D. S., Shapiro Y., Epstein Y., W. Matthew, and Pandolf K. B.: A modified discomfort index (MDI) as an alternative to the wet bulb globe temperature (WBGT), in: Hodgdon J. A. and Heany J. H. (eds.), (in press, 1998).

Moran D. S., Shitzer A., and Pandolf K. B.: A physiological strain index (PSI) to evaluate heat stress. in: Hodgdon J. A. and Heany J. H. (eds.), (in press, 1998).

Moran D. S., Shapiro Y., Laor A., and Pandolf K. B.: Interaction between the physiological strain index (PSI) and sweat electrolyte composition. . *Proc. 9th Int. Conf. Environ. Ergo*. Werner J., Hexamer M., and Mietzsch E. (eds.). Bochum, Germany, 2000.

e. Invited Seminars or Colloquiums

1. "Heat Strokes and Heat Illnesses", Invited Seminar, Human Performance Laboratory and Sport Laboratory for People with Disabilities, University of Connecticut, March 12th, 1998.

2. "Israeli Heat Stroke Experience" Invited lecture, "The 1998 Current Concepts of Operational Environmental Medicine" - An Army Medical Department Postgraduate Professional Course, Natick, MA, May 5th, 1998

3. "Hyperthermia and Hypothermia: Illness/Injury" invited lecture in Symposia: "The Environment and Exercise". The XXVI FIMS World Congress of Sport Medicine, Orlando, FL, June 3rd, 1998.

4. "Heat and cold strain indexes" Invited seminar, Defense and Civil Institute of Environmental Medicine, North York, Ontario, Canada, December 15th, 1998.

5. "Acclimatization and Heat Tolerance Test" Invited seminar, Defense and Civil Institute of Environmental Medicine, North York, Ontario, Canada, December 15th, 1998.

6. "The Israeli Army Heat Stroke Experience" Invited lecture, "The 1999 Current Concepts of Operational Environmental Medicine" - An Army Medical Department Postgraduate Professional Course, New Orleans, MA, May 5th, 1999.

7. "Predictive Models and Indices of Physiological Strain for the Heat and the Cold" a Mini-Symposium, The 46th Annual Meeting of American College of Sports Medicine, Seattle, OR, June 2-5, 1999.

8. "Physiological strain indices to evaluate heat and cold stresses" Invited seminar, US Army Institute of Environmental Medicine, Natick, MA, June 16th, 1999.

f. Abstracts presented at Scientific Meetings

Moran D. S. and Pandolf K. B.: A physiological stress index (PSI) for evaluation of protective gear. *The Israel - USA R&D Symposium "Shoresh"*, Zichron Yaakov, April, 1998.

Moran D. S., Laor A., Epstein Y., and Shapiro Y.: A modified discomfort index (MDI) asa substitute for the wet bulb globe temperature (WBGT). *Med. Sci. Sports Exerc.* 30: S284 (#1615), 1998.

Moran D. S. Shapiro Y., Epstein Y., and Pandolf K. B.: A modified discomfort index (MDI) as an alternative to the wet bulb globe temperature (WBGT). *8th Int. Conf. Environ. Ergo.* San Diego, CA, Oct., 1998.

Moran D. S., Shitzer A., and Pandolf K. B.: A physiological strain index (PSI) to evaluate heat stress. *8th Int. Conf. Environ. Ergo.,* San Diego, CA, Oct., 1998.

Moran D. S., Epstein Y., and Shapiro Y.: Biochemical profile changes during exertional heat stroke. *8th Int. Conf. Environ. Ergo.,* San Diego, CA, Oct., 1998.

Pandolf K. B., Moran D. S., Laor A., Izraeli S., Gerecht D., and Shapiro Y.: Can gender differences during exercise-heat stress be assessed by the physiological strain index? *Med. Sci. Sports Exerc.* 30: Sxxx (#xxx), 1999.

Pandolf K. B., Tikuisis P., and Moran D. S.: Predictive models and indices of physiological strain for the heat and the cold. *Med. Sci. Sports Exerc.* 30: Sxxx (#xxx), 1999.

Moran D. S., Castellani J. W., O'Brien, Young A. J., and Pandolf K. B.: A cold strain index (CSI) to evaluate physiological strain during cold exposure. *Med. Sci. Sports Exerc.* 30: Sxxx (#xxx), 1999.

Moran D. S., Shapiro Y., Laor A., and Pandolf K. B.: Interaction between the physiological strain index (PSI) and sweat electrolyte composition. *9th Int. Conf. Environ. Ergo.*, Bochum, Germany, July, 2000.

Report By Shin-Lin Chen Ph.D.

10/13/98

Date: October 8, 1998

Name: Shin-Lin Chen

Name of Laboratory or Center and Location: USAMRIID, Fort Detrick, Maryland

Dates of Tenure: October 1, 1997 to October 18, 1998

Title of Research Proposal: Development of a cell-free assay for the inhibition of Ebola virus replication

Name of research advisor: Dr. John Huggins

Are you on leave from a professional post? No

Professional Society Offices held during tenure: N/A

Professional travel during tenure: None

Seminars or lectures delivered at Universities and/or Institutes: None

Summary of research during tenure:

I have identified a clone containing Ebola L gene ORF by RTPCR using total RNA isolated from Ebola viral lysate and specifically designed primer. This ORF was subcloned into PET expression vector for overexpressing L protein. But due to very low expressioin, I subcloned L gene ORF into pBacPAKHis2 vector and use Baculovirus expression system for over-expressing L protein. VP35 and NP proteins were over-expressed by PET expressioin system and purified by His-bind resin. RNA binding assay indicates Ebola NP protein can bind to GFP(green fluorescence protein) antisense mRNA non-specifically.

Research in progress:

I am transfecting the insect cell lines SF-21 and High Five using recombinant clone containing Ebola L ORF to isolate single plaque for large scale plaque preparation and L protein purification. In order to perform the in vitro assay under non-isotopic condition, I have prepared DIG-11-UTP and Biotin-16-UTP labeled mRNAs from pEbozminiGFP containing 5' and 3' untranslated regiion of Ebola RNA genome and GFP ORF in between, and pGEMGFP containing only GFP ORF. I will perform RNA binding assay using Ebola NP protein and non-isotopic mRNA probes, and detected by anti-DIG antibody and ELISA using TMB agent.

Publications and papers resulting from NRC associateship research: None

Presentations at scienfitic meetings or conferences: None

Patent or copyright applicatiions resulting from NRC associateship research: None

Future position and address and/or forwarding address

USPTO Patent Examiner
Address: US Patent and Trademark Office
2011 Crystal Drive, Suite 707
Washington, DC 20231
Forwarding address(Please mail tax statement to this address):
8232 Skipwith Drive
Frederick, MD 21702

Appraisal of the associateship programs

NRC associateship program provides me a very good opportunity to explore in the molecular virology field and is helpful in my career. I am really appreciated of what this program has given me.

NRC RESEARCH ASSOCIATESHIP PROGRAM

REPORT

DATE: November 2, 1998

NAME: Mary C. Guttieri

LAB OR CENTER: USAMRIID, Ft. Detrick, MD

DATES OF TENURE: October 5, 1995-November 5, 1998

TITLE OF RESEARCH PROPOSAL:

Production and Examination of Mouse and Human Monoclonal Antibodies to Hantaan and Puumala viruses using a Baculovirus Expression System

RESEARCH ADVISOR: Dr. Connie Schmaljohn

LEAVE FROM PROFESSIONAL POST: none

PROFESSIONAL SOCIETY OFFICES: none

PROFESSIONAL TRAVEL:

American Society for Virology 15th Annual Meeting
London, Ontario, Canada
July 13-17, 1996

American Society of Tropical Medicine and Hygiene
Baltimore, Maryland
December 1-5, 1996

SEMINARS OR LECTURES AT UNIVERSITIES AND/OR INSTITUTES: none

SUMMARY OF RESEARCH:

I conducted passive protection experiments in hamsters to determine the protective efficacy of a baculovirus-expressed human monoclonal antibody to Puumala virus. The results of these studies indicated that this antibody does not fully protect animals from challenge with Puumala virus. I conducted an extensive analysis of human hybridomas generated from the spleens of transgenic mice and determined that none secrete Hantaan-specific monoclonal antibodies. I developed a system to select human B cells

producing hantavirus-specific antibodies by using antigen coated magnetic beads. I determined the complete nucleotide sequence of a previously cloned Fc-containing gene region and designed a strategy to construct cassette plasmid vectors containing human signal sequences and an Fc antibody coding region. I conducted extensive analysis of stably-transformed insect cell lines expressing a human IgG MAb to the G2 protein of Puumala virus and developed a strategy to determine the copy number of heavy and light chain antibody genes integrated within transformed insect cell genomes.

RESEARCH IN PROGRESS:

I am completing studies to determine the copy number of heavy and light antibody genes within transformed insect cells. I am analyzing immortalized B cell lines to attempt to identify those expressing hantavirus-specific antibodies. Specific cells of interest will be selected and cloned using magnetic bead technology. I am completing the construction of a combinatorial library using Fab antibody genes amplified from the peripheral blood of a Puumala-virus infected individual. I am beginning construction of Fc cassette plasmid vectors.

PUBLICATIONS AND PAPERS:

(a) Publications in peer-reviewed journals

Liang, M., M. Guttieri, A. Lundkvist, and C. Schmaljohn. 1997. Baculovirus expression of a human G2-specific, neutralizing IgG monoclonal antibody to Puumala virus. *Virology* **235**:252-260.

(b) Books or book chapters

(c) Manuscripts in preparation

Guttieri, M.C., C. Bookwalter, M. Liang, A. Lundkvist, and C. Schmaljohn. 1998. Expression of a human G2-specific, neutralizing monoclonal antibody to Puumala virus in stably transformed lepidopteran cells. (in preparation).

PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES:

Guttieri, M., M. Liang, A. Lundkvist, and C. Schmaljohn. 1996. Baculovirus expression of a human G2-specific, neutralizing monoclonal antibody to Puumala virus. ASV 15th Annual Meeting, London, Ontario, Canada.

Guttieri, M.C., M. Liang, A. Lundkvist, and C.S. Schmaljohn. 1996. Baculovirus expression of a human G2-specific, neutralizing monoclonal antibody to Puumala virus. ASTMH 45th Annual Meeting, Baltimore, MD.

Guttieri, M.C., C.S. Bookwalter, A. Lundkvist, and C.S. Schmaljohn. 1998. Expression of a human G2-specific, neutralizing monoclonal antibody to Puumala virus in stably transformed Lepidopteran cells. Conference on Emergence and Control of Rodent-Borne Viral Diseases, Annecy, France.

PATENT OR COPYRIGHT APPLICATIONS: none

FUTURE POSITION TITLE AND STATUS:

Title: Technical Professional V (government contractor)

Location: USAMRIID, Ft. Detrick--in the laboratory of Dr. Connie Schmaljohn

FORWARDING ADDRESS:

Dr. Mary C. Guttieri
1005-2A Columbine Drive
Frederick, MD 21701

APPRAISAL OF THE ASSOCIATESHIP PROGRAMS:

I am grateful for the research opportunities afforded me by the NRC associateship program. During my tenure, I acquired knowledge and expertise in areas defined as "cutting edge technology", equipping me with valuable research skills in a competitive market. The administrative staff was both very courteous and helpful. Assistance was always offered in a kind and timely manner. As for improvement, I feel that there is a definite need to increase the maximum length of tenure from 3 years to 4 or 5 years. This adjustment would allow for the proper completion of important projects, manuscripts, and presentations.

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

National Research Council
Associateship Programs

REPORT FORM

If you have downloaded this form, enter the information electronically.
Return this form directly to the NRC as an e-mail attachment or print out and mail.

1) NAME

Steven J. Hatfill

2) DATE

August 11, 1999

3) *Program / Agency*		*Lab / Center*	*Location*
	or enter abbreviation		
click on prgm/agnc	**RIID**	**Antiviral therapeutic**	**USAMRIID**

4) DATES OF TENURE

September 15, 1997 -- to – September 17, 1999

5) NAME OF RESEARCH ADVISER

John Huggins

6) IF YOU ARE ON LEAVE FROM A PROFESSIONAL POST, WILL YOU RETURN TO YOUR PREVIOUS EMPLOYER?

☐ Yes ☒ No

7) PROFESSIONAL AWARDS RECEIVED, SOCIETY OFFICES HELD DURING TENURE

nil

8) PROFESSIONAL TRAVEL DURING TENURE **List locations and dates of travel to scientific meetings; group into domestic and foreign.**

nil

9) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES **List location(s) and date(s).**

Council on Foreign Relations-May 21, 1998
Potomac Institute for Policy Studies/George Washington University-June 16, 1998
Pentagon, Assistant Secretary of Defense SO/LIC-July 14, 1998
Pentagon, Assistant Secretary of Defense for Health Affairs-August 11, 1998
DoD Worldwide Conference on Antiterrorism-August 24,1998

10) TITLE OF RESEARCH PROPOSAL

Pathogenesis of the Coagulopathy associated with Filovirus Infections

11) SUMMARY OF RESEARCH DURING TENURE **Itemize significant findings in concise form (25 words/250 characters each item.) Utilize concepts and key words.**

1) **Identification of early intrinsic pathway coagulation abnormality in Ebola Non-Human Primate infection.**
2) **Documentation of equivelent Ebola-induced coagulopathy in murine and guinea pig models.**
3) **Documentation of pathogenic differences in human tissues infected with Ebola Zaire and Reston strains**
4) **Documentation of transient coagulopathy in Monkeypox infected non-human primates.**
5) **Applications of NASA RWV for advanced Orthopoxvirus research.**
6) **Efficacy of Cidofovir in minimizing pulmonary damage in Orthopoxvirus infection.**
7)
5)

12) RESEARCH IN PROGRESS **Briefly describe in 100 words or less.**

Use of PAGE to document abnormal von Willebrand multimers during early Ebola Zaire induced coagulopathy in non-human primates.
Utilization of the NASA RWV system to study camelpox infection of human lung tissue, and the development of this culture system to document cytokine changes in human lymphoid tissue infected with Orthopoxvirus.

13) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH
Provide complete citation(s) including author(s), full name of journal, volume number, page number(s), year of publication.

(a) Publications in peer-reviewed journals:

(b) Books or book chapters:

Textbook of Aerospace Medicine-USAF-Aeromedical Evacuation

(c) Manuscripts in preparation, manuscripts submitted:

Pathogenic differences between Ebola Reston and Ebola Zaire in the NASA RWV Bioreactor
Coagulation in Mouse, Guinea Pig and Non-Human Primate models of Ebola Zaire
Cidofovir treatment for Orthopoxvirus infections

14) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES
Provide complete reference with author(s), title, abstract/proceeding citation, meeting name, location. Group into domestic and foreign.

Bray,M., Jaax,N., Geisbert,T., Kell,W., Hatfill,S.,Huggins,J. pathogenesis of Lethal Ebola Virus Infection in Adult Immunocompetent Mice. American Society of Virology, Annual Meeting, Vancouver, canada, july 11, 1998.

15) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH
Provide titles, authors, and dates of applications.

nil

16) NEW POSITION STATUS/CATEGORY **Please indicate only one.**

- ☐ *Research -- National Government* (U.S. or Foreign)
- ☐ *Administration -- U.S. Govt.* (Fed., State, or Local)
- ☐ *Continuation at Host Lab/Center*
  Abbreviate Host Lab/Center: _____
- ☐ *College/University*
- ☐ *Postdoctorate*
- ☒ *Self Employment*
- ☐ *Non Profit*
- ☐ *Industry*
- ☐ *Other*
  Please specify:

17) NEW POSITION TITLE AND NAME (not address) OF ORGANIZATION

N/A

18) FORWARDING ADDRESS **(to which your tax statement will be mailed)**

1711 W. 7th Street, Apt 9
Detrick Plaza Apartments
Frederick, MD 21702

19) APPRAISAL OF THE ASSOCIATESHIP PROGRAM
Please evaluate each of the following on a scale of 1 (poor) to 10 (excellent):

10 a) Of what value was this experience to your career?

10 b) What is your evaluation of your experience in the laboratory?

10 c) What is your evaluation of your interaction with the NRC?

Please provide any additional comments on the usefulness of the Associateship Program to you, including suggestions for improvements.

The NRC Associate Program is outstanding and is really a national asset, both with respect to individual career advancement as well as providing assistance to National civilian and Department of Defense research programs.

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Washington, DC 20007

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

REPORT FORM
RESEARCH ASSOCIATESHIP PROGRAMS

If you have downloaded this, you may print out and enter the information manually, or you may enter the information electronically, then return as an e-mail attachment.

1) NAME

Kurt I. Kamrud

2) DATE

June 18, 1999

3) *Program / Agency*	*Lab / Center*	*Location*
or enter abbreviation		
click on prgm/agnc **AMRDC**	**AMRIID**	**Fort Detrick**

4) DATES OF TENURE

August 5, 1996 -- to – June 30, 1999

5) NAME OF RESEARCH ADVISER

Dr. Connie Schmaljohn

6) IF YOU ARE ON LEAVE FROM A PROFESSIONAL POST, WILL YOU RETURN TO YOUR PREVIOUS EMPLOYER?

☐ Yes ☒ No

7) PROFESSIONAL AWARDS RECEIVED, SOCIETY OFFICES HELD DURING TENURE

American Committee on Arthropod-borne Viruses, Scherer-Hardy Award - 1997

8) PROFESSIONAL TRAVEL DURING TENURE **List location(s) and date(s) of travel to scientific meetings; group into domestic and foreign.**

American Society for Virology, Monatana, July 1997
American Society of Tropical Medicine and Hygiene, Florida, December 1997
International Conference on Negative Strand Viruses, Ireland, September 1997
International Conference on HFRS and Hantaviruses, Georgia, March 1998
Emergence and Control of Rodent-borne Viral Diseases, France, October 1998
Vaccine Research Conference, Wahington D.C., March 1999

9) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES **List location(s) and date(s).**

University of Deleware , September 1996

10) TITLE OF RESEARCH PROPOSAL

Development and Comparison of Three Recombinant Vaccines to Puumala Virus

11) SUMMARY OF RESEARCH DURING TENURE **Itemize significant findings in concise form. Utilize concepts and key words.**

1) Develop and test DNA-based Sindbis replicon vectors for Hantavirus vaccinces

2) Develop and test DNA-based vectors for Hantavirus vaccines

3) Develop and test packaged Sindbis replicon vector for Hantavirus vaccines

4) Demonstrate protective efficacy of all three vaccine vectors for Hantaviruses

5)

12) RESEARCH IN PROGRESS **Briefly describe in 100 words or less.**

Characterization of protective efficacy of each vaccine vector completed for Seoul virus. Vectors are in the process of being modified to contain structual protein genes for all of the pathogenic members of the Hantavirus genus.

13) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH
Provide complete citation(s) including author(s), full name of journal, volume number, page number(s), year of publication.

(a) Publications in peer-reviewed journals:

Hooper, J.W., Kamrud, K.I., Elgh F., Custer, D., and Schmaljohn, C.S. 1999. DN Vaccination with Hantavirus M Segment Elicits Neutralizing Anti. ies and Protects against Seoul Virus Infectio. irology 255:269-278.

(b) Books or book chapters:

Schmaljohn, C.S., Kamrud, K.I., and Hooper, J.W. 1999. Recombinant DNA Vaccines for Hantaviruses. In: Factors in the Emergence and Control of Rodent-Borne Diseases (Saluzzo, J.F. and Dodet, B. eds). Elsevier, Paris (In press).

Kamrud, K.I. and Schmaljohn, C.S. 1999. Hantaviruses. In: Emerging and Reemerging Infectious Diseases. (Olive, M. eds). Eaton Publishing, Natick, MA. (Submitted).

(c) Manuscripts in preparation, manuscripts submitted:

Kamrud, K.I., Hooper, J.W., Elgh, F., and Schmaljohn, C.S. 1999. Comparison of Naked DNA, DNA-based Sindbis Replicon, and Packaged Sindbis Replicon Vectors Expressing Hantavirus Structural Genes in Hamsters. Virology (Submitted).

Ma M., Kersten, D.B., Kamrud, K.I., Wool-Lewis, R.J., Schmaljohn, C.S., and Gonzalez-Scarano, F. 1999. Pseudotyping of Murine Leukemia Virus with Glycoprotein from La Crosse Virus and Hantaan Virus. Virus Research (In press).

14) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete reference with author(s), title, abstract/proceeding citation, meeting name, location. Group into domestic and foreign.

4th International Conference on HFRS and Hantaviruses. 1998. K. Kamrud, T. Nelle, F. Elgh, L. VanderZanden, K. Anderson, and C. Schmaljohn "Evaluation of Naked DNA and Alphavirus Based Hantavirus Vaccines". Atlanta, Georgia.

Emergence and Control of Rodent-Borne Viral Diseases (Hantaviruses and Arenaviruses). 1998. K. Kamrud, J. Hooper, F. Elgh, and C. Schmaljohn "Packaged Sindbis Virus Replicons as Potential Hantavirus Vaccine Vectors". Les Pensieres, Veyrier-du-Lac, France.

NCI-FCRDC/Fort Detrick Spring Research Festival. 1999. K. Kamrud, J. Hooper, F. Elgh, and C. Schmaljohn "Comparison of the Immunogenicity and Protective Efficacy of Naked-DNA, DNA-based Sindbis Replicons, and Packaged Sindbis Replicon Vectors Expressing Seoul Virus Structural Genes in Hamsters". Frederick, Maryland.

15) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

16) NEW POSITION TITLE, ORGANIZATION and ADDRESS

Microbiologist, USAMRIID, Virology Division, Fort Detrick, Frederick, MD 21702

17) NEW POSITION PLANS **You may indicate more than one.**

- ☒ *Research -- National Government* (U.S. or Foreign)
- ☐ *Administration -- U.S. Govt.* (Fed., State, or Local)
- ☐ *Remain at Host Lab/Center*
- ☐ *College/University Professor*
- ☐ *Postdoctoral*
- ☐ *Uncertain*
- ☐ *Self-Employed*
- ☐ *Industry*
- ☐ *Other*

(Please provide name of Host Lab/Center.)

18) FORWARDING ADDRESS **(to which your tax statement will be mailed)**

6320 Towncrest Ct. Frederick, MD 21703

19) APPRAISAL OF THE ASSOCIATESHIP PROGRAM

Please evaluate each of the following on a scale of 1 (poor) to 10 (excellent):

10 a) Of what value was this experience to your career?

10 b) What is your evaluation of your experience in the laboratory?

10 c) What is your evaluation of your interaction with the NRC?

Please provide any additional comments on the usefulness of the Associateship Program to you, including suggestions for improvements.

The NRC Associateship program is excellent. I have only two comments. 1) Reimbursement of travel expenses was slow (ranging from 2-4 months) after travel was completed. Many times registration and accomodations costs had to be payed out 3 to 4 months in advance of the meeting, resulting in output of personal funds without compensation of up to half a year. A more streamlined method of reimbursement should be adopted to avoid such long delays in distribution of travel funds. 2) A clerical error in salary on the part of someone in the NRC in 1999 (or late 1998), resulted in the program having to collect back a portion of the salary over a 3 month period from all NRC associates at USAMRIID (perhaps other institutes as well?). Every effort

should be made NOT to repeat this fiscal behavior. It reflects poorly on the program as it resulted in a great deal of financial difficulty over that period of time. I sincerely hope that the indivdual(s) responsible for this mistake were reprimanded and made aware of the repercussions of their actions.

USPS Mailing Address	FAX Number	Express-Delivery Address
Associateship Programs [TJ 2114]	202 – 334 – 2759	Associateship Programs [Suite 2114]
NATIONAL RESEARCH COUNCIL	INTERNET	NATIONAL RESEARCH COUNCIL
2101 Constitution Avenue, NW	national-academies.org/rap	1000 Thomas Jefferson Street, NW
Washington, DC 20418		Washington, DC 20007

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ID. # Copy To / Date Cost-Center #